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EDITORS
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CHAPTER 1

FREE RADICAL SCAVENGING ACTIVITIES OF MIXED LIGAND CU (II) AMINO ACID COMPLEXES

Assoc. Prof. Dr. Duygu İNCİ ÖZBAĞCI[1]

1 Assoc. Prof. Dr. Duygu İNCİ ÖZBAĞCI

INTRODUCTION

Coordination complexes play a significant role in boinorganic chemistry and have a wide research area because of their structures, chemical reactions, colours, abundance, and magnetic properties. Nowadays, coordination complexes are widely used in dyestuff, in explaining biological phenomena in medicine, in removing the hardness of water, in the synthesis of substances with biological activity and in industry. Free radicals are atoms or molecules that contain one or more unshared electrons. Because these radicals have lost one electron from their outermost electron shell, these radicals want to share the electrons of other atoms to compensate for this electron gap (Halliwell and Gutteridge, 1990). The uncontrolled proliferation of radicals in living organisms could pose a great danger to living things. Antioxidants are complexes that neutralize free radicals and stop or slow down their oxidation. Antioxidants restrict lipid oxidation by accumulating reactive oxygen species. (Halliwell and Gutteridge, 1990; Halliwell, 1994)

Various analytical methods are applied to determine the antioxidant properties of compounds. In these methods, chemical principles are valid and while an antioxidant may show highly antioxidant activity with a selected measurement procedure, the same antioxidant may show a lower activity with another method. For this reason, at least two procedures should be used to define and compare the antioxidant capacities of synthetic or natural antioxidants. There are different analytical methods developed to measure antioxidant capacity. In order to say that a compound has a 'high antioxidant capacity', it must be determined by more than one method and compared with other compounds. The aim of this study is to determine the radical scavenging activities of Cu(II) complexes previously synthesized and characterized by our group ($\{[Cu(phen)(trp)]ClO_4 \cdot 3H_2O\}_n$ (1), $\{[Cu(4\text{-}mphen)(trp)]ClO_4 \cdot 3H_2O\}_n$ (2), $[[Cu\ (dmphen)(trp)(MeOH)][Cu(dmphen)(trp)(NO_3)]]NO_3$ (3), $[Cu(phen)(gln)(H_2O)]NO_3.H_2O$ (4), $[Cu(dmphen)(gln)(H_2O)]ClO_4$ (5), $[Cu(nphen)(asn)]ClO_4)_n$ (6) and $[Cu(nphen)(gln)(H_2O)]\ ClO_4.H_2O$ (7)) and to compare them with standard antioxidants (**İnci et al., 2017; Şenel et al., 2019; Kiraz et al, 2019**).

ANTIOXIDANTS

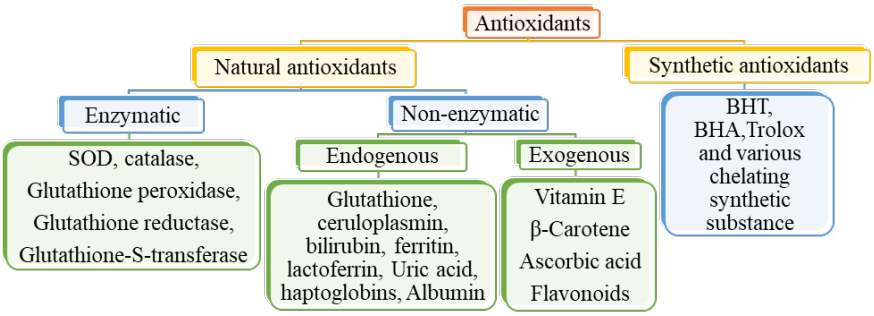


Figure 1. *Classification of antioxidants*

METHODS USED TO DETERMINE ANTIOXIDANT CAPACITY

With the understanding of the importance of antioxidants, the number of studies on this subject has increased day by day. Antioxidant activity determination methods are based on two basic principles. The first of these is the analyses based on "Hydrogen Atom Transfer" (HAT) and the second is the analyses based on "Electron Transfer" (ET). The main assays based on the HAT reaction mechanism are radical-trapping antioxidant parameter (TRAP) and oxygen radical absorbance capacity (ORAC). The main analyses based on the ET reaction mechanism are the total antioxidant efficiency determination method by ferric thiocyanate (FTC) method, Trolox equivalent antioxidant capacity method (ABTS/TEAC), cupric ion (Cu^{2+}) reduction antioxidant capacity method (CUPRAC), iron ions reduction antioxidant capacity method (FRAP), DPPH radical scavenging activity determination and applied for total phenolic substance amount analysis is the Folin-Ciocalteu method (Apak et al., 2007).

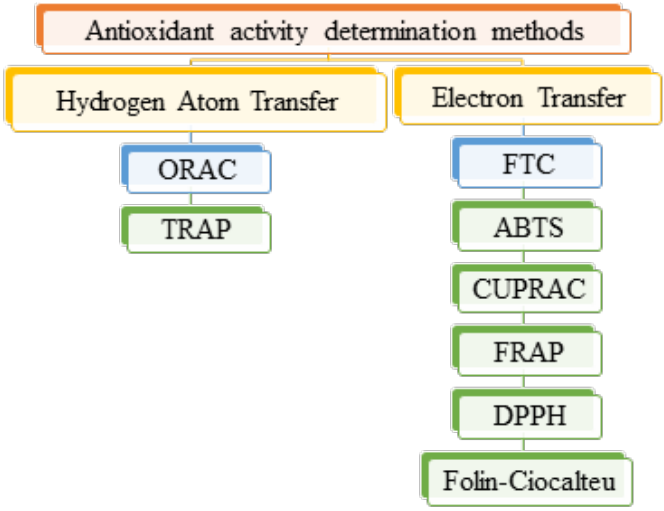


Figure 2. *Antioxidant activity determination methods*

FREE RADICALS

Free radicals are atoms or molecules that can be ions or neutral, containing an unshared electron in their outermost orbital. These molecules, which are highly reactive, can be formed during the biochemical reactions of the organism or due to external factors. Free radicals, with their strong reactive properties, can cause irreversible damage to all cellular molecules and macromolecules, enzyme systems, and compounds of biochemical importance. Hydroxyl and superoxide radicals can especially damage membrane systems (Belyurt, 2014).

Table 1. *Free radicals and the properties of some free radical-producing species*

Name	Symbol	Property
Hydrogen radical	$H^{\bullet}$	The simplest known radical
Hydroxyl radical	$OH^{\bullet}$	The most reactive oxygen metabolite radical. It attacks all molecules in the human body.
Superoxide radical	$O_2^{\bullet-}$	First intermediate product of oxygen metabolism
Hydrogen peroxide	H_2O_2	It has low reactivity and poor molecular damage properties.
Singlet oxygen	O_2	Short half-life, strong oxidative form
Perhydroxy radical	$HO_2^{\bullet-}$	It dissolves rapidly in lipids and increases lipid peroxidation.
Peroxyl radical	$ROO^{\bullet-}$	It is weaker than perhydroxyl and lyses into lipids.
Trichloromethyl radical	$CCl_3^{\bullet}$	It is a product of CCl_4 metabolism, a radical produced in the liver.
Thiyl radical	$RS^{\bullet}$	It is the general name for species containing sulphur and unpaired electrons.
Alkoxyl radical	$RO^{\bullet}$	It is an oxygen metabolite produced by the breakdown of organic peroxides.
Nitrogen monoxide	NO	Produced in vivo from L-arginine
Nitrogen dioxide	NO_2	It is produced from the reaction of NO with oxygen. It is also found in polluted air, cigarette smoke, etc.

AMINO ACIDS and *N,N*-DONOR LIGANDS

An amino acid consists of a hydrogen atom bonded to the central carbon atom, an amino group, a carboxyl group, and a functional group symbolized by “R”. This functional group determines the diversity of amino acids. Amino acids are known as the building blocks of proteins that are responsible for vital activities. Amino acids that participate in the structure of proteins can have different functions on their own.

Donor atoms that bond with the central metal ion of amino acids; The amino group is the nitrogen atoms, and the carboxyl is the oxygen atom. Donor atoms in the R group in the structure of amino acids can also participate in coordination with the metal ion. For example, the sulphur atom in the L-cysteine functional group, the nitrogen atom in the imidazole ring in the L-histidine functional group, the carboxyl oxygen atom in the functional group in L-aspartic acid and L-glutamic acid can coordinate to the central metal ion. Possible binding models of amino acids to metal ions are shown in Figure 3.

In the most observed binding model of amino acids, it shows bidentate ligand behaviour by binding from the carboxyl oxygen and nitrogen of the amino group. In another binding model of amino acids, they exhibit tridentate ligand behaviour by binding to the metal ion via the carbonyl oxygen atom as well as the carboxyl oxygen and amino group nitrogen. Amino acids also show bidentate ligand behaviour by binding to the metal ion via the carboxyl oxygen and the carbonyl oxygen in the carboxyl group. In another coordination model in which amino acids bind to the metal ion,

it exhibits tetradentate ligand behaviour. In addition, amino acids act as monodentate ligands by binding to the metal ion only from the nitrogen atom of the amino group or the oxygen atom in the carboxyl group.

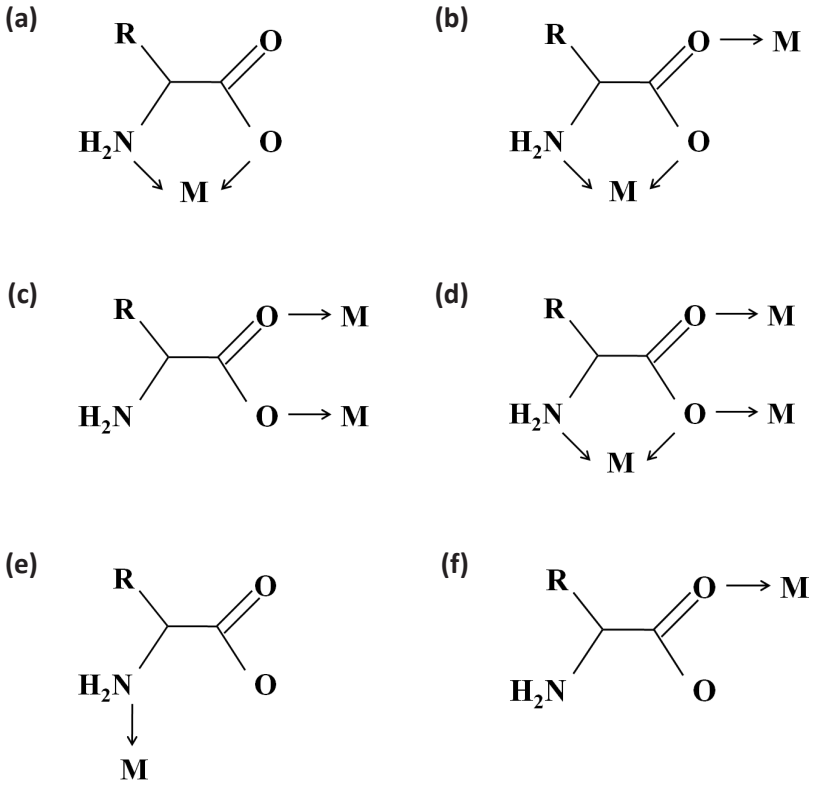
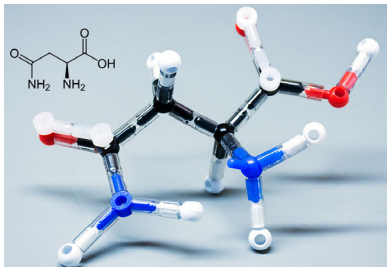
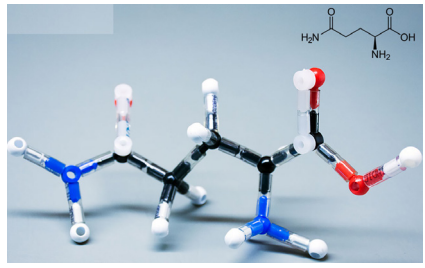


Figure 3. *Possible coordination forms of amino acid complexes*

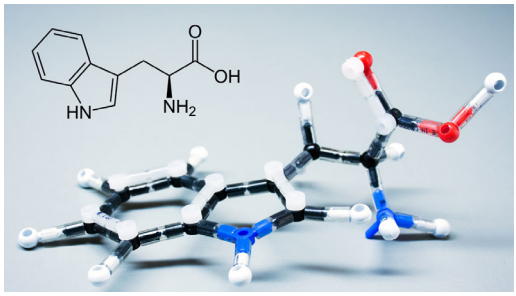
In this study, the amino acids in the structure of the complexes of which radical scavenging activity was investigated: Tryptophan, glutamine, and asparagine. Acidic amino acids have a negatively charged R group in their functional side chains. Aspartic acid and glutamic acid are in this group (Figure 4). The difference between glutamic acid and aspartic acid is that it has an extra $–CH_2$ group in its structure. The ion form of aspartic acid is aspartate, and the ion form of glutamic acid is glutamate. The amide forms of aspartic acid and glutamic acid are asparagine and glutamine. Their functional group side chains contain an amide group, and their side chains are uncharged. Asparagine and glutamine can easily be converted into aspartic acid and glutamic acid forms with acid or base. The amide group in the functional group has a polar structure and can make H-bonds.



Asparagine (asn)



Glutamine (gln)



Tryptophan (trp)

Figure 4. *The structure of asn, gln and trp*

N,N-donor atoms in the structure of the complexes (1-7) of which radical scavenging activity was investigated in this study: 1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-methyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline (Figure 5). 1,10-phenanthroline (phen) has played a significant role in the progress of coordination chemistry, is a ligand that can chelate transition metal ions with two donor nitrogen and continues to gain importance as a versatile ligand in many fields such as organic, inorganic and supramolecular chemistry. (Sammes and Yahioğlu 1994). Phen has a planar, hydrophobic and electron-poor heteroaromatic structure. These structural properties define the coordination ability against metal ions. The reason for the increased interest in the complexes formed by phen and its derivatives with metal ions recently is that they can show biological activity as a result of their interactions with biomolecules (Alessino et al. 1997). Phen and its derivatives offer a wide variety of biological and technological applications. Therefore, it is important to investigate the synthesis and application areas of complexes containing phen and its derivatives.

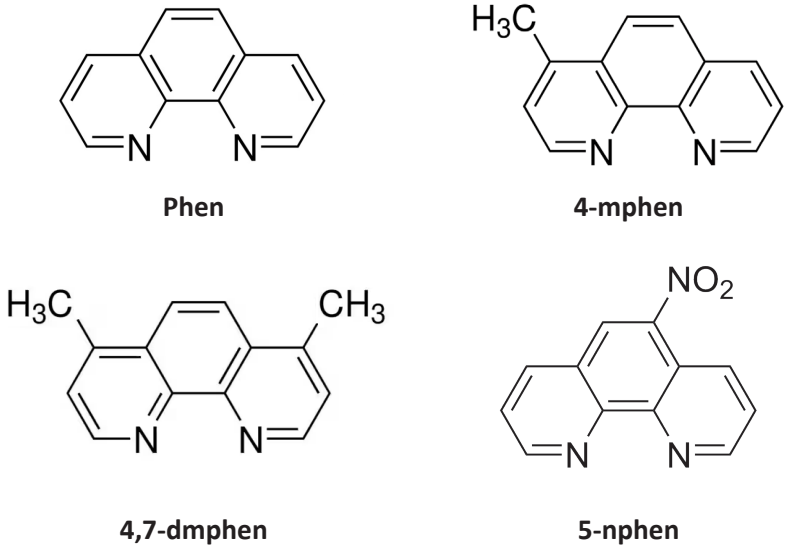
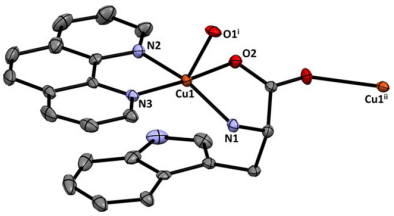
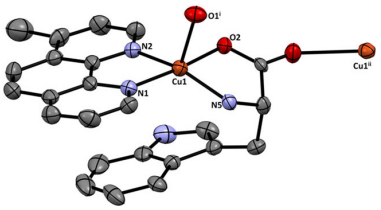
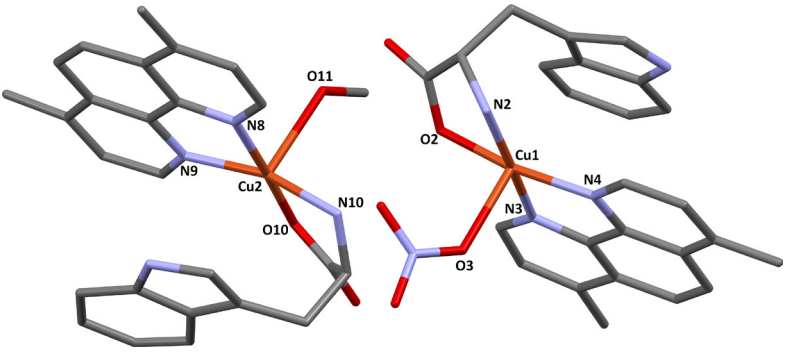
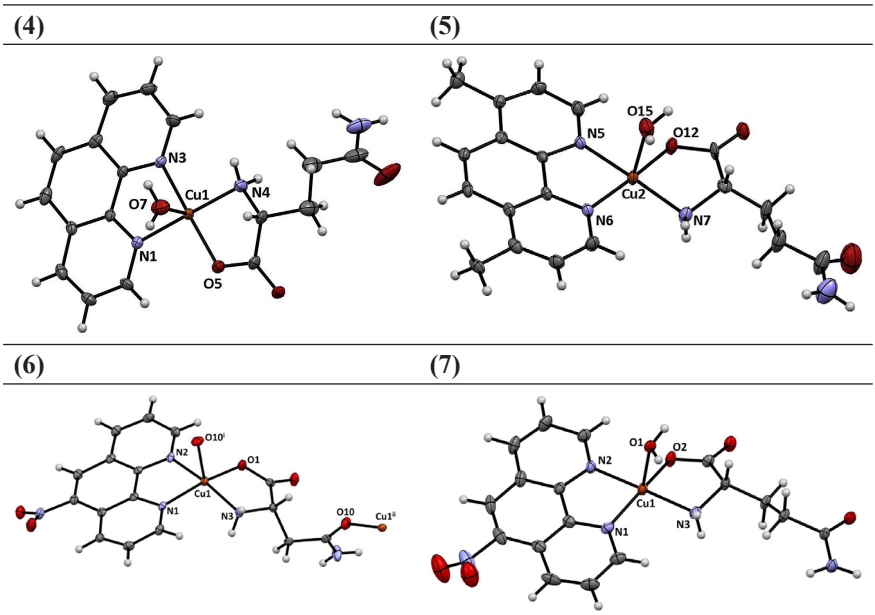


Figure 5. *The structure of phen, 4-mphen, 4,7-dmphen and 5-nphen*

Table 2. *The Cu(II) complexes (1-7) investigated in the study (İnci et al., 2017; Şenel et al., 2019; Kiraz et al, 2019)*

(1)	(2)
	
(3)	
	



INVESTIGATION OF DPPH RADICAL SCAVENGING ACTIVITY

This procedure was first proposed by Blois (1958). It is one of the most widely used antioxidant methods for plant and organic molecule samples. DPPH· (2,2-diphenyl-1picrylhydrazyl) is a stable radical that can react with complexes that could donate hydrogen atoms and creates a maximum absorbance at 517 nm. Antioxidant activity is given by the IC_{50} (effective concentration) value, which expresses the amount of antioxidant consumed to reduce the initial DPPH concentration by 50 % (Brand-Williams et al., 1995). DPPH radical scavenging method is an easy, economical, fast, efficient method that is widely used to measure antioxidant efficiency and especially to evaluate the radical scavenging activity of nonenzymatic antioxidants (İlhami, 2020).

Cu(II) complexes (1-7) in different concentration ranges were added to the ethanol solution of DPPH and shaken vigorously by vortex. After being kept in the dark for 30 min, the absorbance was read at 517 nm. Percent inhibition was calculated from the following formula:

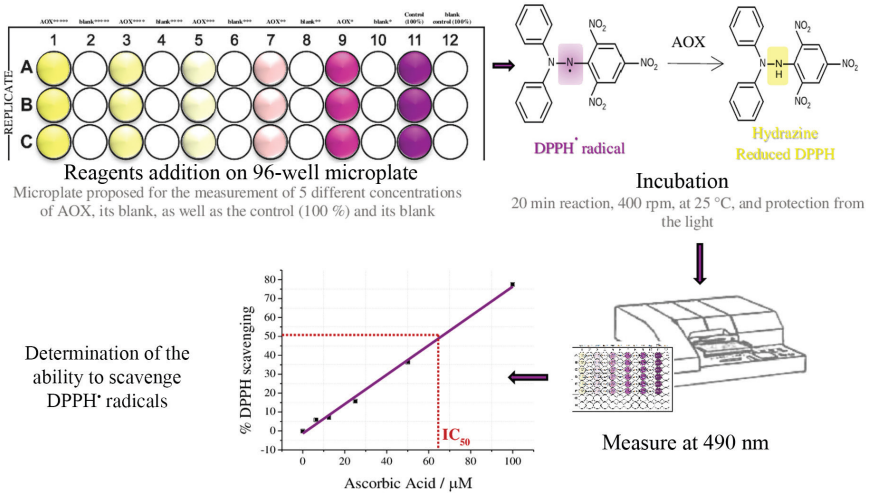


Figure 6. *Schematic representation of the DPPH method (Becker et al., 2019)*

IC_{50} values of DPPH radical scavenging activities obtained for the Cu(II) complexes (1-7) and standard antioxidants are given in Table 3. According to the results obtained from the DPPH radical scavenging activities of Cu(II) complexes (1-7), when the antioxidant activities of the complexes are compared with ascorbic acid used as standards, **(3)** has the highest activity among the complexes (Figure 7). Compared to β-carotene, all complexes (1-7) were found to have higher DPPH radical scavenging activity.

Table 3. *The radical scavenging activities of the Cu(II) complexes*

IC_{50} (µM)	
Compounds	**DPPH**
(**1**)	159.8 ± 0.06
(**2**)	121.8 ± 0.03
(**3**)	22.8 ± 0.09
(**4**)	364.1 ± 0.13
(**5**)	118.2 ± 0.07
(**6**)	324.8 ± 0.23
(**7**)	400.6 ± 0.09
Ascorbic acid	25.6[a]
Trolox	7.73[a]
BHT	15.04[a]
β-carotene	415.3[b]

(*: This study, [a]: İnci et al., 2019, [b]: Rahman et al., 2015)

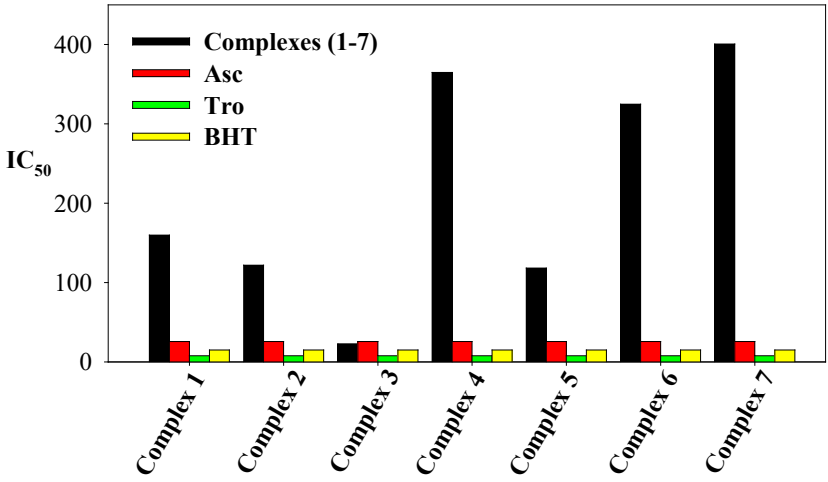


Figure 7. *The radical scavenging activities of the Cu(II) complexes (1-7)*

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CHAPTER 2

ABSOLUTE TRIBONACCI SERIES SPACE AND ITS MATRIX OPERATORS

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INTRODUCTION

From the past to the present, one of the most fundamental concepts in mathematics is the notion of sequences\series. The concept of convergence of series, which is well known today, actually dates back to ancient times. When the concept of convergence had not yet been defined, mathematicians have obtained some contradictory results by performing arbitrary operations to obtain the sum of the series and have not been able to overcome the contradictions for a long time. While some of the existing contradictions have been resolved using Gauss's binomial theorem, Cauchy, who had studied on this field, has formulated the notion of convergence of a sequence (or series) and provided a new perspective. This has been the origin of the concepts of divergence and convergence of sequences (or series) as they are known today. Although Cauchy's definition eliminated many uncertainties at that time, it brought the following question to mind: Could the divergent series have a sum? The answer to this problem is given by extending the notion of convergence. Thus the theory of summability was born. Let us examine the following example, which summarises the basis of the topic in a simple way: taking $u = -1$ in the following formula (actually we have known that the formula provides $|u| < 1$)

$$1 + u + u^2 + \cdots = \frac{1}{1-u} \ ,$$

the equality

$$1 - 1 + 1 - 1 + \cdots = \frac{1}{2} \qquad (1)$$

has been obtained by Euler.

Actually, there is a fault in terms of the concept of Cauchy convergence in this equality, because the series $\sum_{k=0}^{\infty}(-1)^k$ is divergent. On the other hand, if the transformation sequence is produced via the first order Cesàro mean of the sequence (s_m) which is the sequence of partial sum of that series, then it is obtained as follows:

$$t_m = \frac{1}{m+1}\sum_{k=0}^{m} s_k$$
$$= \frac{1}{2} + \frac{1}{4(m+1)}[1 + (-1)^m].$$

Here, it is clear that (t_m) converges to $1/2$, $m \to \infty$. Hence, the sum of the non-convergent series given by (1) is calculated as 1/2 using the Cesàro summability method. This example shows that divergent series can be summed, if the method is changed, so it is very important in terms of summabilty theory.

The summability theory continues to play an important role in many areas of science. For example, this theory and and its related subfields are often used in engineering sciences, applied mathematics, and especially in analysis (functional analysis, calculus, Fourier analysis,…) The theory of sequence space together with matrix transformations, defined between two sequence spaces, is one of the main topics of summability theory. This theory is mainly concerned with the generalizations of the concept of convergence for sequences and series. Within this framework, it is aimed to give a limit to non-convergent series or sequences with the help of a transformation determined by the most general linear mappings of infinite matrices. The answer to the question why the concept of matrix is used for a general linear operator is that a linear operator between two sequence spaces can be given by an infinite matrix. In this respect, the literature on the summability theory continues to expand, on the one hand, in the construction, properties and matrix operators of sequence\sequence spaces obtained as the domain of a special matrix, such as Hausdorff, Hölder, Fibonacci, Cesaro, Nörlund and Euler matrices, and on the other hand, in the study of new sequence spaces derived by various absolute summability methods from a different point of view. (For example, Dağlı& Yaying, 2023; Gökçe, 2022; Gökçe, 2021; Gökçe & Sarıgöl,2020; Gökçe & Sarıgöl, 2019; Gökçe & Sarıgöl, 2019a; Gökçe & Sarıgöl,2018; Gökçe & Sarıgöl, 2018a; Gökçe (in press); Ilkhan, 2020; Yaying& Kara, 2021; Yaying&Hazarika,2020).

Recently, the series spaces $|T_\theta|_q$ and $|T_\theta|(\varphi)$ have been introduced as the sets of all series summable by the absolute Tribonacci method related to the spaces l_q and $l(\varphi)$, respectively, and studied their several properties (Gökçe (in press)). The main purpose of this study is to give the necessary and sufficient conditions for $\Lambda\epsilon\ \left(U, |T_\theta|(\varphi)\right)$ and

$\Lambda\epsilon(|T_\theta|(\varphi),\Gamma)$, where U is any sequence space and $\Gamma=\{c,c_0,l_\infty\}$ after examining some important algebraic and topological properties of the paranormed absolute Tribonacci series space.

First of all, there is a reminder of some familiar concepts. ω is the set of all complex sequences. Any vector subspace of ω is called a sequence space. In this sense, l_∞ , c, c_0 are examples of well-known sequence spaces, representing the sets of all bounded, convergent and null sequences. Similarly, c_s, b_s represent the spaces of all bounded and convergent series.

Assume that $U,V\subset\omega$, $\Lambda=(\lambda_{nv})$ is an arbitrary infinite matrix of complex components. If the series

$$\Lambda_n(x)=\sum_{v=0}^{\infty}\lambda_{nv}u_v$$

converges for $u\epsilon U$ and for all $n\epsilon\mathbb{N}=\{0,1,2,3,\dots\}$, then, Λ-transform of the sequence $u=(u_v)$ is denoted by $\Lambda(u)=(\Lambda_n(u))$. Besides, it is said that Λ describes a matrix transformation from U into V, and it is shown with $\Lambda\epsilon\,(U,V)$ or $\Lambda\colon U\to V$ if $\Lambda(u)=(\Lambda_n(u))\epsilon\,V$ for every $u\epsilon\,U$.

The notions of domain of an infinite matrix Λ in U is identified by the set

$$U_\Lambda=\{\mathrm{u}=(u_n)\epsilon\,\omega:\Lambda(\mathrm{u})\epsilon\,\mathrm{U}\},\qquad(2)$$

it is noted immediately that this set is a sequence space like U.

If $t_{nv}=0$ for $v>n$ and otherwise $t_{nv}\neq 0$ for all n,v, then the matrix $T=(t_{nv})$ is called a triangle.

A linear topological space (also called a topological vector space) is both of a topological space and a vector space such that the properties of scalar multiplication and vector addition are continuous. Assume that U is a topological vector space over $\mathbb{R}$. For all $a\,\epsilon\mathbb{R}$ and $\tilde{u},u\epsilon\,U$, if

- $f\colon U\to\mathbb{R}$ such that $f(0)=0, f(u)=f(-u)$
- $f(u+\tilde{u})\leq f(u)+f(\tilde{u})$
- $|a_n-a|\to 0$, $f(u_n-u)\to 0$ imply $f(a_nu_n-au)\to 0$ as $n\to\infty$, that is the scalar multiplication is continuous

then, it is said that U is a paranormed space.

Assume that $U\subset\omega$. If U is a Frechet space with continuous coordinates $R_n\colon U\to\mathbb{C}$ described by $R_n(u)=u_n$ for all $u\epsilon\,U,n\epsilon\mathbb{N}$, then U is called an FK-space. Moreover, if the metric of an FK-space also

determines a norm, then it is said to be a BK-space. These notions play an important role in the theory of summability. For example, matrix transformations between FK-spaces are continuous. Another important concept in the literature of the summability theory is the Schauder base: it is said that an FK-space U has a Shauder base (b_v) if there exists unique sequence of coefficient (u_v) such that

$$\lim_{j\to\infty}\sum_{v=0}^{j} u_v b_v = u,$$

for all $u\epsilon U$.

To give an example of these concepts, Maddox space, which is presented as follows

$$l(\varphi) = \left\{x = (x_n): \sum_{n=0}^{\infty} |x_n|^{\varphi_n} < \infty\right\}.$$

is an FK-space with its natural paranorm

$$f(x) = \left(\sum_{n=0}^{\infty} |x_n|^{\varphi_n}\right)^{1/\mathrm{H}}$$

where $H = max\left\{1, \sup_n \varphi_n\right\}$ and also the sequence $(e^{(v)})$ whose terms given by

$$e_n^{(v)} = \begin{cases} 1, & n = v \\ 0, & n \neq v \end{cases}$$

for $v \geq 0$, is the Shauder base of the Maddox space $l(\mu)$. On the other side, if $\varphi_n \geq 1$ for all n, the Maddox space $l(\varphi)$ becomes a BK- space with the norm

$$\|u\| = inf\left\{\xi > 0: \sum_{n=0}^{\infty} |u_n/\xi|^{\varphi_n} \leq 1\right\},$$

(Maddox, 1969,1968,1967).

During the whole study, we assume that (θ_n) is any sequence of positive numbers, $\varphi = (\varphi_n)$ is arbitrary bounded sequence of positive real numbers, $0 < inf\,\varphi_n \leq K < \infty$, and φ_n^* is the conjugate of φ_n such that $1/\varphi_n^* + 1/\varphi_n = 1$ for $\varphi_n > 0$, $1/\varphi_n^* = 0$ for $\varphi_n = 1$.

Tribonacci numbers, like Fibonacci and Lucas numbers, are very interesting. A number of studies involving these numbers have taken palce in the literature. Tribonacci numbers are sequence of integers identified the third order recurrence relation with initial conditions

$$t_0 = 1, t_1 = 1, t_2 = 2,$$
$$t_v = t_{v-1} + t_{v-2} + t_{v-3},$$
$$t_{-v} = 0, v > 0.$$

So, some of the first Tribonacci numbers can be listed as follows:

$$1, 1, 2, 4, 7, 13, 24, 44\ldots.$$

Besides, Tribonacci numbers have useful properties as follows:

$$\sum_{v=0}^{n} t_v = \frac{t_{n+2} + t_n - 1}{2},$$
$$\sum_{v=0}^{n} t_{2v} = \frac{t_{2n+1} + t_{2n} - 1}{2},$$
$$\lim_{n\to\infty} \frac{t_n}{t_{n+1}} = 0.54368901 \ldots.$$

In addition to these properties, Tribonacci matrix $T = (t_{nv})$ has recently been defined by Yaying and Hazarika (2020) as follows:

$$t_{nv} = \begin{cases} \dfrac{2t_v}{t_{n+2} + t_n - 1}, & 0 \le v \le n \\ 0, & v > n \end{cases}$$

where t_v be the vth Tribonacci number for every $v \epsilon \mathbb{N}$.

Let take an infinite series $\sum a_v$ and the sequence $s = (s_n)$ which is its nth partial sum, and also let $\theta = (\theta_n)$ be any sequence of positive real numbers, $\varphi = (\varphi_n)$ be a bounded sequence of positive real numbers. If

$$\sum_{n=1}^{\infty} \theta_n^{\varphi_{n-1}} |\Lambda_n(s) - \Lambda_{n-1}(s)|^{\varphi_n} < \infty,$$

the series $\sum a_v$ is said to be summable $|\Lambda, \theta_n|(\varphi)$ (Gökçe & Sarıgöl, 2018a). It should be seen immediately that the summability $|\Lambda, \theta_n|(\varphi)$ includes a lot of summability methods for special cases of the matrix Λ and the sequences θ, μ. To give a few examples: if we decide on the weighted mean matrix instead of Λ, the summability method $|\Lambda, \theta_n|(\mu)$ is reduced

to $|\bar{N}, p_n, \theta_n|(\varphi)$ and the set of all series summable by the method is given by

$$|\bar{N}_p^{\theta}|(\varphi) = \left\{ a = (a_v) : \sum_{n=1}^{\infty} \theta_n^{\varphi_n - 1} \left| \frac{p_n}{P_n P_{n-1}} \sum_{v=1}^{n} P_{v-1} a_v \right|^{\varphi_n} < \infty \right\},$$

(Gökçe & Sarıgöl, 2018a), if we decide on the Fibonacci matrix instead of Λ with $\theta_n = n$ for all n, the method is reduced to $|F, \theta_n|(\varphi)$ and the set of all series that can be summed by the absolute Fibonacci summability method is obtained as

$$|F_{\theta}|(\varphi) = \left\{ a = (a_v) : \sum_{n=1}^{\infty} \theta_n^{\varphi_n - 1} \left| \sum_{v=0}^{n} \sigma_{nv} a_v \right|^{\varphi_n} < \infty \right\},$$

(Gökçe & Sarıgöl, 2020), if we decide on the Euler matrix instead of Λ, the method is reduced to $|E^r, \theta_n|(\varphi)$ and the set of all series that can be summed by the absolute Euler method is determined as follows:

$$|E_{\theta}^{r}|(\varphi) = \left\{ a = (a_v) : \sum_{n=1}^{\infty} \theta_n^{\varphi_{n-1}} \left| \sum_{v=1}^{n} \binom{n-1}{v-1} (1-r)^{n-v} r^{v} a_v \right|^{\varphi_n} < \infty \right\},$$

(Gökçe & Sarıgöl, 2018), if we decide on the Cesàro matrix instead of Λ with $\theta_n = n$ for all n, the method is reduced to $|C, \alpha, \beta|(\varphi)$ and the set of all series summable by this method is given by :

$$\left|C_{\lambda,\mu}\right|(\varphi)=\left\{a=(a_v):\sum_{n=1}^{\infty}n^{\varphi_n-1}\left|\sum_{v=0}^{n}\left(\frac{A_{n-v}^{\lambda-1}}{A_n^{\lambda+\mu}}-\frac{A_{n-v-1}^{\lambda-1}}{A_{n-1}^{\lambda+\mu}}\right)A_v^{\mu}s_v\right|^{\varphi_n}<\infty\right\}$$

(Gökçe & Sarıgöl, 2019). We can also refer the reader to studies (Gökçe, 2022; Gökçe, 2022a; Gökçe & Sarıgöl, 2019a; Güleç, 2023; Mohapatra & Sarıgöl, 2018).

Also, if we choose the Tribonacci matrix instead of Λ, the summability method $|\Lambda,\theta_n|(\varphi)$ is reduced to the summability method $|T,\theta|(\varphi)$. Besides, the set of all series summable by $|T,\theta|(\varphi)$ can be present as

$$|T_\theta|(\varphi)=\left\{u:\sum_{n=0}^{\infty}\theta_n^{\varphi_n-1}\left|\frac{2t_n}{t_{n+2}+t_n-1}u_n+\sum_{j=0}^{n-1}u_j\left(\frac{2t_n}{t_{n+2}+t_n-1}+\Delta\sigma_n\sum_{v=j}^{n-1}2t_v\right)\right|^{\varphi_n}<\infty\right\},$$

(Gökçe, (in press)).

Finally, before the main theorems, we state some useful lemmas:

Lemma 1.1 (Grosse-Erdmann,1993) Assume that $\varphi=(\varphi_v)$ is a bounded sequences of strictly positive numbers.

(i) if $\varphi_n\le 1$ for all n, then,

$$\Lambda\in(l(\varphi),c)\Leftrightarrow(i)\ \lim_{n\to\infty}\lambda_{nv}\ \text{exists for each } v,\quad(ii)\ \sup_{n,v}|\lambda_{nv}|^{\varphi_v}<\infty$$

$$\Lambda\in(l(\varphi),c_0)\Leftrightarrow(iii)\ \lim_{n\to\infty}\lambda_{nv}=0\ \text{ for each } v,\qquad(ii)\ \text{holds}$$

$$\Lambda\in(l(\varphi),l_\infty)\Leftrightarrow(ii)\ \text{holds.}$$

(ii) if $\varphi_n>1$ for all n, then,

$\Lambda \in (l(\varphi), c)$
$\Leftrightarrow (i')$ $\lim_{n\to\infty} \lambda_{nv}$ exists for all v,
(ii') there exists a number $M > 1$ such that
$\sup_n \sum_{v=0}^{\infty} |\lambda_{nv} M^{-1}|^{\varphi_v^*} < \infty$,
$\Lambda \in (l(\varphi), c_0) \Leftrightarrow (iii')$ $\lim_{n\to\infty} \lambda_{nv} = 0$ for each v,
(ii') holds
$\Lambda \in (l(\varphi), c_0) \Leftrightarrow (ii')$ holds.

Lemma 1.2. (Malkowsky & Rakocevic, 2000) Let R be a triangle. Then, for $U, V \subset \omega, \Lambda \in (U, V_R)$ iff $B = R\Lambda \in (U, V)$.

Lemma 1.3. (Malkowsky & Rakocevic, 2007) Let U be an FK-space with AK property, $V \subset \omega$. Also, let R be a triangle with its inverse S. Then, $\Lambda \in (U_R, V)$ iff $\tilde{\Lambda} \in (U, V)$ and $V^{(n)} \in (U, c)$ for all n, where

$$\tilde{\lambda}_{nv} = \sum_{j=v}^{\infty} \lambda_{nj} s_{jv}, n, v = 0,1, \ldots$$

$$v_{mv}^{(n)} = \begin{cases} \sum_{j=v}^{m} \lambda_{nj} s_{jv}, 0 \le v \le m \\ 0, \quad v > m. \end{cases}$$

Lemma 1.4. (Malkowsky & Rakocevic, 2007) Let (U, d) be a linear metric space with its basis $\left(b^{(n)}\right)$. Then, the sequence $\left(S(b^{(n)})\right)$ is also basis of $V = U_R$ with the metric d_R described by $d_R(v, \hat{v}) = d(R(v), R(\hat{v}))$ for all $v, \hat{v} \in V$.

Lemma 1.5. (Wilansky, 1984) Assume that U and V are BK-spaces, and Λ is any infinite matrix of complex components. If $\Lambda \in (U, V)$, then it is said that Λ determines a bounded linear operator.

ABOUT THE ABSOLUTE TRIBONACCI SPACE $|T_\theta|(\varphi)$

In this part of the article, we will first establish the absolute Tribonacci summability method combining the concepts of absolute summability and Tribonacci matrix. To obtain this method, let us take the sequence $\sum u_v$ and its partial sums s_n. Then we get

$$\Lambda_n(s) = \sum_{j=0}^{n} t_{nj} s_j = \sum_{v=0}^{n} u_v \sum_{j=v}^{n} \boldsymbol{t}_{nj} = \sum_{v=0}^{n} u_v \sum_{j=v}^{n} \frac{2t_j}{t_{n+2} + t_n - 1}$$

and so,

$$\Delta\Lambda_n(s) = \sum_{v=0}^{n} u_v \sum_{j=v}^{n} \frac{2t_j}{t_{n+2} + t_n - 1} - \sum_{v=0}^{n-1} u_v \sum_{j=v}^{n-1} \frac{2t_j}{t_{n+2} + t_n - 1}$$

$$= \frac{2t_n}{t_{n+2} + t_n - 1} u_n + \sum_{v=0}^{n-1} u_v \left(\frac{2t_n}{t_{n+2} + t_n - 1} + \Delta\sigma_n \sum_{j=v}^{n-1} 2t_j \right)$$

$$= \sum_{v=0}^{n} u_v \, \Phi_{nv}$$

where

$$\Phi_{nv} = \begin{cases} \dfrac{2t_n}{t_{n+2} + t_n - 1}, & v = n \\ \dfrac{2t_n}{t_{n+2} + t_n - 1} + \Delta\sigma_n \displaystyle\sum_{j=v}^{n-1} 2t_j, & 0 \le v \le n-1 \\ 0, & v > n \end{cases}$$

$$\Delta\sigma_n = \sigma_n - \sigma_{n-1}, \sigma_n = \frac{1}{t_{n+2} + t_n - 1}.$$

Now, we are ready to present the absolute Tribonacci space as the set of all series summable by $|T, \theta|(\varphi)$ as follows:

$$|T_\theta|(\varphi) = \left\{ u \in \omega : \sum_{n=0}^{\infty} \theta_n^{\varphi_n - 1} \left| \sum_{j=0}^{n} u_j \, \Phi_{nj} \right|^{\varphi_n} < \infty \right\}.$$

Also, it is seen immediately that,

$$(E^{(\varphi)} \circ \tilde{T})_n(u) = \theta_n^{1/\varphi_n^*} (\tilde{T}_n(u) - \tilde{T}_{n-1}(u))$$

where

$$\tilde{t}_{nv} = \begin{cases} \sigma_n \sum_{j=v}^{n} 2t_j, & 0 \le v \le n \\ 0, & v > n, \end{cases} \quad (3)$$

$$e_{nv}^{(\varphi)} = \begin{cases} -\theta_n^{1/\varphi_n^*}, & v = n-1 \\ \theta_n^{1/\varphi_n^*}, & v = n \\ 0, & v \neq n-1, n. \end{cases} \quad (4)$$

With this information and the notation of domain, the space redefines as $|T_\theta|(\varphi) = \left(l(\varphi)\right)_{(E^{(\varphi)} \circ \tilde{T}}$.

Also, it is known that there exists unique inverse matrix which also is a triangle for every triangle matrix. So, the matrices $E^{(\varphi)}$ and $\tilde{T}$ have inverse matrices whose terms is given by

$$\left(e_{nj}^{(\varphi)}\right)^{-1} = \begin{cases} \theta_j^{-1/\varphi_j^*}, & 0 \le j \le n \\ 0, & j > n, \end{cases}$$

$$\tilde{t}_{nj}^{-1} = \begin{cases} \dfrac{1}{2\sigma_n t_n}, & j = n \\ -\dfrac{1}{2\sigma_{n-1}t_n} - \dfrac{1}{2\sigma_{n-1}t_{n-1}}, & j = n-1 \\ \dfrac{1}{2\sigma_{n-2}t_{n-1}}, & j = n-2 \\ 0, & \text{otherwise.} \end{cases}$$

Now, we begin to present the theorems which give us some topological and algebraic properties of the space $|T_\theta|(\varphi)$.

Theorem 2.1

(a) The set $|T_\theta|(\varphi)$ is a linear space with the scalar multiplication and coordinate-wise addition. Furthermore, the space becomes an *FK*-space together with the following paranorm

$$\|u\|_{|T_\theta|(\varphi)} = \left\| E^{(\varphi)} \circ \tilde{T}(u) \right\|_{l(\varphi)} = \left(\sum_{n=0}^{\infty} |u|^{\varphi_n} \right)^{\frac{1}{H}}$$

where $H = max\{1, \sup_n \varphi_n\}$.

(b) If $\varphi_n = q$ for all $n\epsilon\mathbb{N}$, the space $|T_\theta|(\varphi)$ is a *BK*-spaces with the following norm

$$\|u\|_{|T_\theta|(\varphi)} = \left\| E^{(q)} \circ \tilde{T}(u) \right\|_q.$$

Proof.

The first part of the proof is a standard verification, therefore it is omitted. Since the matrices $E^{(\varphi)}, \tilde{T}$ are triangles, it is obvious that the composite function $E^{(\varphi)} \circ \tilde{T}$ is also triangle. Hence, since $l(\varphi)$ is an *FK*-space, then it can be written from the Theorem 4.3.2 in (Wilansky,1984) that $|T_\theta|(\varphi) = \left(l(\varphi)\right)_{E^{(\varphi)} \circ \tilde{T}}$ is also an *FK*-space which concludes the proof of theorem.

Taking $\varphi_n = q$ for all $n\epsilon\mathbb{N}$, it is seen immediately that the space $|T_\theta|(\varphi)$ is reduced to $|T_\theta|_q$ which is studied by Gökçe (Gökçe (in press)). Although we do not include the proof of this part, we can say that it can be proved by a similar method.

Theorem 2.2 The space$|T_\theta|(\varphi)$ has a Schauder basis $b^{(j)}$ whose terms are given by

$$b_n^{(j)} = \begin{cases} \theta_j^{-1/\varphi_j^*} \left(\frac{1}{2\sigma_n t_n} - \frac{1}{2\sigma_{n-1} t_n} - \frac{1}{2\sigma_{n-1} t_{n-1}} - \frac{1}{2\sigma_{n-2} t_{n-1}} \right), & j \le n-2 \\ \theta_{n-1}^{-1/\varphi_{n-1}^*} \left(\frac{1}{2\sigma_n t_n} - \frac{1}{2\sigma_{n-1} t_n} - \frac{1}{2\sigma_{n-1} t_{n-1}} \right), & j = n-1 \\ \theta_n^{-1/\varphi_n^*} \frac{1}{2\sigma_n t_n}, & j = n \\ 0, & j > n. \end{cases}$$

Proof. Since $(e^{(j)})$ is the Schauder base of the Maddox's space $l(\varphi)$, it follows from Lemma 1.4, $b^{(j)} = (\tilde{T}_n^{-1}((E^{(\varphi)})^{-1}(e^{(j)}))$ is the Schauder base of the space $|T_\theta|(\varphi)$.

If we consider the Theorem 2.1 and Theorem 2.2, it is obtained immediately that the absolute series space $|T_\theta|(\varphi)$ is a separable space.

Theorem 2.3. There exists a linearly isomorphism between the spaces $|T_\theta|(\varphi)$ and $l(\varphi)$ i.e., $|T_\theta|(\varphi) \cong l(\varphi)$.

Proof. Let take into account the transformations $\tilde{T}: |T_\theta|(\varphi) \to \left(l(\varphi)\right)_{E^{(\varphi)}}$, $E^{(\varphi)}: \left(l(\varphi)\right)_{E^{(\varphi)}} \to l(\varphi)$ and the matrices corresponding to them defined by (3) and (4). Since these matrices are triangles, it is obvious that the composite matrix $E^{(\varphi)} \circ \tilde{T}$ is also triangle. So, it is obtained immediately that $E^{(\varphi)} \circ \tilde{T}$ is a linear bijective operator. Also,

$$\|u\|_{|T_\theta|(\varphi)} = \left\| E^{(\varphi)} \circ \tilde{T}(u) \right\|_{l(\varphi)}$$

that is, the paranorm is preserved which completes the proof.

SOME MATRIX OPERATORS RELATED TO $|T_\theta|(\varphi)$

In this part of the study, we investigate the characterizations of the matrix classes $\left(U, |T_\theta|(\varphi)\right)$ and $(|T_\theta|(\varphi), \Gamma)$, where $\Gamma = \{c, c_0, l_\infty\}$.

Theorem 3.1 Assume that $\Lambda = (\lambda_{nv})$ is arbitrary infinite matrix of complex number, $\varphi = (\varphi_n)$ is any bounded sequences of positive numbers for $n \epsilon \mathbb{N}$, Also, $H = (h_{nv})$ be a matrix satisfying the following relation

$$h_{nv} = \theta_n^{1/\varphi_v^*} \sum_{j=0}^{n} \Phi_{nj} \lambda_{jv}. \qquad (5)$$

Then, $\Lambda \in \left(U, |T_\theta|(\varphi)\right)$ iff $H \in \left(U, l(\varphi)\right)$.

Proof. Let take $u \in U$. Considering the equation (5), it is written

$$H_n(u) = \sum_{v=0}^{\infty} h_{nv} u_v = \theta_n^{\frac{1}{\varphi_v^*}} \sum_{j=0}^{n} \Phi_{nj} \sum_{v=0}^{\infty} \lambda_{jv} u_v,$$

and also it is seen immediately that $H_n(u) = (E^{(\varphi)} \circ \tilde{T})_n(\Lambda(u))$ for $u \in U$. So, $H_n(u) \epsilon l(\varphi)$ whenever $u \in U$ equals to $\Lambda_n(u) \epsilon |T_\theta|(\varphi)$ whenever $u \in U$. So, it is completed the proof of the theorem.

Theorem 3.2. Let $\Lambda = (\lambda_{nv})$ be an infinite matrix of complex components and $\varphi = (\varphi_n)$ be arbitrary bounded sequence of positive real numbers with $\varphi_v \leq 1$ for each v. Then

(a) $\Lambda \in (|T_\theta|(\varphi), c)$ iff, for all $v \geq 1$

$$\sum_{j=v+2}^{\infty} \lambda_{nj} \left(\frac{1}{2t_j} \Delta\left(\frac{1}{\sigma_j}\right) - \frac{1}{2t_{j-1}} \Delta\left(\frac{1}{\sigma_{j-1}}\right) \right) \text{converges for all } v, \tag{6}$$

$$\sup_{m,v} \left(\left| \theta_v^{-1/\varphi_v^*} \xi_{mv}^{(n)} \right|^{\varphi_v} + \left| \theta_{m-1}^{-1/\varphi_{m-1}^*} \left(\left(\frac{1}{2t_m} \Delta\left(\frac{1}{\sigma_m}\right) - \frac{1}{2\sigma_{m-1}t_{m-1}} \right) \lambda_{nm} + \frac{\lambda_{n,m-1}}{2\sigma_{m-1}t_{m-1}} \right) \right|^{\varphi_{m-1}} + \left| \theta_m^{-1/\mu_v^*} \frac{\lambda_{nm}}{2\sigma_m t_m} \right|^{\varphi_m} \right) < \infty \tag{7}$$

$$\lim_{n\to\infty} \left(\lambda_{nv} \frac{1}{2\sigma_v t_v} + \left(\frac{1}{2t_{v+1}} \Delta\left(\frac{1}{\sigma_{v+1}}\right) - \frac{1}{2\sigma_v t_v} \right) \lambda_{nv+1} + \sum_{j=v+2}^{\infty} \lambda_{nj} \left(\frac{1}{2t_j} \Delta\left(\frac{1}{\sigma_j}\right) - \frac{1}{2t_{j-1}} \Delta\left(\frac{1}{\sigma_{j-1}}\right) \right) \right) \text{exists} \tag{8}$$

$$\sup_{n,v} \left\{ \left| \theta_v^{-1/\varphi_v^*} \left(\lambda_{nv} \frac{1}{2\sigma_v t_v} + \left(\frac{1}{2t_{v+1}} \Delta\left(\frac{1}{\sigma_{v+1}}\right) - \frac{1}{2\sigma_v t_v} \right) \lambda_{nv+1} + \sum_{j=v+2}^{\infty} \lambda_{nj} \left(\frac{1}{2t_j} \Delta\left(\frac{1}{\sigma_j}\right) - \frac{1}{2t_{j-1}} \Delta\left(\frac{1}{\sigma_{j-1}}\right) \right) \right) \right|^{\varphi_v} \right\} < \infty. \tag{9}$$

(a) $\Lambda \in (|T_\theta|(\varphi), c_0)$ iff the conditions (6), (7), (9) hold and

$$\lim_{n\to\infty} \left(\lambda_{nv} \frac{1}{2\sigma_v t_v} + \left(\frac{1}{2t_{v+1}} \Delta\left(\frac{1}{\sigma_{v+1}}\right) - \frac{1}{2\sigma_v t_v} \right) \lambda_{nv+1} \right.$$

$$+\sum_{j=v+2}^{\infty}\lambda_{nj}\left(\frac{1}{2t_j}\Delta\left(\frac{1}{\sigma_j}\right)-\frac{1}{2t_{j-1}}\Delta\left(\frac{1}{\sigma_{j-1}}\right)\right)\Bigg)=0. \quad (10)$$

(c) $\Lambda\in(|T_\theta|(\varphi),l_\infty)$ iff the conditions (6), (7), (9) hold.

Proof Assume that $\varphi_v\le 1$ for each v. Since $|T_\theta|(\varphi)=\left(l(\varphi)\right)_{(E^{(\varphi)}\circ\tilde{T})}$, if we take into account the Lemma 1.3, we get $\Lambda\in(|T_\theta|(\varphi),c)$ if and only if $\widetilde{\Lambda}\in(l(\varphi),c)$ and $V^{(n)}\in(l(\varphi),c)$ where

$$\tilde{\lambda}_{nv}=\theta_v^{-1/\varphi_v^*}\Bigg(\lambda_{nv}\frac{1}{2\sigma_v t_v}+\left(\frac{1}{2\sigma_{v+1}t_{v+1}}-\frac{1}{2\sigma_v t_{v+1}}-\frac{1}{2\sigma_v t_v}\right)\lambda_{nv+1}+\sum_{j=v+2}^{\infty}\lambda_{nj}\left(\frac{1}{2\sigma_j t_j}-\frac{1}{2\sigma_{j-1}t_j}-\frac{1}{2\sigma_{j-1}t_{j-1}}+\frac{1}{2\sigma_{j-2}t_{j-1}}\right)\Bigg)$$

$n,v=0,1,\dots$, and

$$v_{mv}^{(n)}=\begin{cases}\theta_v^{-1/\varphi_v^*}\xi_{mv}^{(n)}, & 0\le v\le\\ \theta_{m-1}^{-1/\varphi_{m-1}^*}\left(\left(\frac{1}{2\sigma_m t_m}-\frac{1}{2\sigma_{m-1}t_m}-\frac{1}{2\sigma_{m-1}t_{m-1}}\right)\lambda_{nm}+\frac{1}{2\sigma_{m-1}t_{m-1}}\lambda_{n,m-1}\right), & v=\\ \theta_m^{-1/\varphi_m^*}\left(\frac{1}{2\sigma_m t_m}\right)\lambda_{nm}, & v=\\ 0, & v>\end{cases}$$

$$\xi_{mv}^{(n)} = \lambda_{nv}\frac{1}{\sigma_v t_v} + \left(\frac{1}{2\sigma_{v+1}t_{v+1}} - \frac{1}{2\sigma_v t_{v+1}} - \frac{1}{2\sigma_v t_v}\right)\lambda_{nv+1} + \sum_{j=v+2}^{m}\lambda_{nj}\left(\frac{1}{2\sigma_j t_j} - \frac{1}{2\sigma_{j-1}t_j} - \frac{1}{2\sigma_{j-1}t_{j-1}} + \frac{1}{2\sigma_{j-2}t_{j-1}}\right).$$

It is clear that by Lemma 2.1, $\widetilde{\Lambda} \in (l(\varphi), c)$ gives us the conditions (8), (9). Moreover, $V^{(n)} \in (l(\varphi), c)$ if and only if (6) and (7) hold. So, this completes the first part of the proof.

Since the remaining part can be proved in similar method, to avoid repetition, it left to the reader.

Theorem 3.3. Assume that $\varphi = (\varphi_n)$ is a bounded sequence of positive real numbers with $\varphi_v > 1$ for all v and $\Lambda = (\lambda_{nv})$ is an infinite matrix of complex components. Then

(a) $\Lambda \in (|T_\theta|(\varphi), c)$ iff, there exists an integer $M > 1$

$$\sup_m \left\{ \left| M^{-1}\theta_{m-1}^{\frac{-1}{\varphi^*_{m-1}}} \left(\left(\frac{1}{2t_m}\Delta\left(\frac{1}{\sigma_m}\right) - \frac{1}{2\sigma_{m-1}t_{m-1}}\right)\lambda_{nm} + \frac{\lambda_{n,m-1}}{2\sigma_{m-1}t_{m-1}} \right) \right|^{\varphi^*_{m-1}} + \left| M^{-1}\theta_m^{-1/\mu_v^*}\frac{\lambda_{nm}}{2\sigma_m t_m} \right|^{\varphi_m^*} + \sum_{v=0}^{m-2} \left| M^{-1}\theta_v^{-1/\varphi_v^*}\xi_{mv}^{(n)} \right|^{\varphi_v^*} \right\} < \infty \quad (11)$$

$$\sup_n \left\{ \sum_{v=0}^{\infty} \left| M^{-1}\theta_v^{-1/\varphi_v^*} \left(\frac{\lambda_{nv}}{2\sigma_v t_v} + \left(\frac{1}{2t_{v+1}}\Delta\left(\frac{1}{\sigma_{v+1}}\right) - \frac{1}{2\sigma_v t_v}\right)\lambda_{nv+1} + \sum_{j=v+2}^{\infty}\lambda_{nj}\left(\frac{1}{2t_j}\Delta\left(\frac{1}{\sigma_j}\right) - \frac{1}{2t_{j-1}}\Delta\left(\frac{1}{\sigma_{j-1}}\right)\right)\right)\right|^{\varphi_v^*} \right\} < \infty \quad (12)$$

and the conditions (6), (8) hold.

(b) $\Lambda \in (|T_\theta|(\varphi), c_0)$ iff the conditions (6), (10), (11) and (12) hold.

(c) $\Lambda \in (|T_\theta|(\varphi), l_\infty)$ iff the conditions (6), (11), (12) hold.

Proof Let $\varphi_v > 1$ for all v. Since $|T_\theta|(\varphi) = \left(l(\varphi)\right)_{(E^{(\varphi)} \circ \tilde{T})}$, it follows from Lemma 2.2 that $\Lambda \in (|T_\theta|(\varphi), c_0)$ if and only if $\widetilde{\Lambda} \in (l(\varphi), c)$ and $V^{(n)} \in (l(\varphi), c)$ where the matrices $\widetilde{\Lambda}$ and $V^{(n)}$ are defined as in the Theorem 3.2. It is written immediately from Lemma 2.1 that $\widetilde{\Lambda} \in (l(\varphi), c_0)$ if and only if (10) and (12) hold. Again, with Lemma 2.1, $V^{(n)} \in (l(\varphi), c)$ if and only if the conditions (6) and (11) hold. So, the proof is completed.

The other part of the theorem can be proved in similar way.

Theorem 3.4. Assume that $\Lambda = (\lambda_{nv})$ is an infnite matrix of complex numbers, $\theta = (\theta_n)$ is any sequence of positive real numbers, $\varphi = (\varphi_n)$ is any bounded sequence of positive numbers and $\Gamma = \{c, c_0, l_\infty\}$. If $\Lambda \in (|T_\theta|(\varphi), \Gamma)$, then Λ determines a bounded linear operator.

Proof. It is known that matrix transformations between *FK*-spaces (or *BK*-spaces) are continuous. So, it can be obtained easily that the matrix operators between the *BK* -spaces c, c_0, l_∞ which are normed *FK*-spaces, and $|T_\theta|(\varphi)$ are bounded linear operators.

In the remaining part of study, we give some results which is obtained with special selections:

Take the matrix $L = (l_{nk})$ as

$$l_{nk} = \begin{cases} 1, & 0 \le k \le n \\ 0, & k > n. \end{cases}$$

Since $b_s = (l_\infty)_L$ and $c_s = (c)_L$, the characterizations of the matrix classes $(|T_\theta|(\varphi), b_s)$ and $(|T_\theta|(\varphi), c_s)$ can listed as follows with Lemma 2.3 :

Corollary 3.5. Put $u(n, v) = \sum_{j=0}^{n} u_{jv}$ instead of u_{nv} in the Theorem 3.2 and Theorem 3.3. Then,

(a) if $\varphi_v \le 1$ for all v,
$(|T_\theta|(\varphi), b_s) \Leftrightarrow$ (6), (7), (9) hold,
$(|T_\theta|(\varphi), c_s) \Leftrightarrow$ (6), (7), (8), (9) hold,

(b) if $\varphi_v > 1$ for all v,
$(|T_\theta|(\varphi), b_s) \Leftrightarrow$ (6), (11), (12) hold,
$(|T_\theta|(\varphi), c_s) \Leftrightarrow$ (6), (8), (11), (12) hold.

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CHAPTER 3

KARMARKAR-TYPE ANISOTROPIC COMPACT STARS IN F(R,Ø,X) GRAVITY

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1. INTRODUCTION

Weyl (1919) and Eddington (1923) establish early attempts in order to introduce to higher-order generalization of General Relativity (GR), in addition that GR appears as a theory that well explains the interaction between matter and geometry of the universe. Especially in recent years, modifications of GR have been proposed, taking into account many different geometrical and mathematical perspectives. It is possible to explain early-time inflation through Starobinsky model in f(R) theory, one of the well-known modification of GR (Starobinsky, 1980). The theory, proposed by Buchdal (1970), contains an additional scalar degree of freedom apart from graviton. Also, the theory gives rise to first internally consistent inflationary consideration model. The other well-known modified theory is f(R,T) gravity. Since Harko *et al.* (2011) produced f(R,T) gravity, many researchers have analysed to cosmological and astrophysical problems through curvature-matter couplings in the theory (Bhattacharjee, 2020; Moraes, 2017; Taser, 2020; Baffou, 2019; Moraes, 2016; Taser, 2021). Recently, another proposed modification of GR is $f(R,\phi,X)$ theory (Bahamonde, 2015). In $f(R,\phi,X)$ theory, Lagrangian density for geometrical part is described with a function including some parameter (Ricci Curvature, field and a kinetic term (Bahamonde, 2015). Due to the properties, it is possible to define several modified models that can be reduced to scalar-tensor and/or $f(R)$-class theories (Cui, 2018). In $f(R,\phi,X)$ theory, late-time acceleration and Λ-CDM evolution are admitted by some specific form of general function (Bahamonde, 2015). Also, it is possible to investigate early-time inflation with viable $f(R,\phi,X)$ functions including Starobinsky model, as well (Bahamonde, 2015). In the toy theory, there are approaches that can offer suggestions to many problems of cosmology that remain to be solved (Wei, 2012; Shamir, 2020; Goncalves and Santos, 2021; Malik *et al.*, 2022a; Malik *et al.*, 2022b; Malik *et al.*, 2023a; Malik *et al.*, 2023b).

On the other hand, stellar examinations are critical tool for understanding internal structure, evolution and physical properties of stars. These examinations help test ability of gravitational theories to produce results compatible with stars and evaluate accuracy of the theories by comparing them with observation data. In this context, there is great numbers of stellar object examinations in modified theories. Karmarkar (1948) determined conditions for class-one Riemannian geometries embedded in n+1 dimensional Euclidien spacetimes. Karmarkar condition

is taken into account many times for study of compact stars (CS) models (Bhar *et al.*, 2016; Maurya and Maharaj, 2017; Mustafa *et al.*, 2020; Naz *et al.*, 2021; Rahaman *et al.*, 2020; Zubair *et al.*, 2022). Maurya *et al.* (2017) suggested new Buchdal-type anisotropic model by using equation of state $p = f(\rho)$ and achieved physical properties of CS such as Her X-1 and RXJ 1856-37. Singh *et al.* (2017) obtained interior solutions for anisotropic star models satisfying Karmarkar conditions. Waheed *et al.* (2020) obtained interior solutions of CS by using the metric which satisfies Karmarkar and Pandey–Sharma conditions together. They analyzed physical properties of obtained solutions by using observational data of Vela X-1 star. Malik *et al.* (2022) researched charged anisotropic CS in $f(R,\phi,X)$ theory by using Krori-Barua spacetime. They investigated stability conditions of such stars and compared observational data for physical viability. From TOV (Tolman-Oppenheimer-Volkoff) equation, Carvalho *et al.* (2015) showed relation between mass and radius of CS. Govender *et al.* (2020) studied dissipative gravitationally collapse of an initially static star which satisfies Karmarkar condition. Sharma *et al.* (2021) generalized Buchdahl compactness limit for a special class of anisotropic stars. Prasad *et al.* (2019) studied physical viability and stability of anisotropic CS models with Karmarkar condition in General Relativity. Malik *et al.* (2023a) investigated strange quintessence anisotropic stars by using Krori-Barua spacetime in $f(R,\phi,X)$ gravity.

This study aims to investigate whether Karmarkar-type line-element model constructs anisotropic CS in the context of $f(R,\phi,X)$ theory. In the literature, there are Krori-Barua Type and CS studies which have a general form which meets the Karmarkar condition, researched within the scope of $f(R,\phi,X)$ theory. In this study, we consider a star model, different from the star models considered in the literature and/or corresponds to a special case, that meets the Karmarkar condition and is accepted in the literature. On the other hand, in order to compare the accuracy of the results obtained, we also considered the sample stars whose data were used, other than those used in the literature. Firstly, field equations for $f(R,\phi,X)$ theory is refreshed in Sec. 2. After that, field equations for spherically symmetric space-time satisfying Karmarkar condition with anisotropic fluid are attained in $f(R,\phi,X)$ theory. By considering specific form of H function with Klein-Gordon equation, we get solutions for constructed model. Considered line element constants satisfying Karmarkar condition by using matching limits are examined for obtained model. All solutions apply to

some CS such as PSR J1614-2230, 4U 1820-30, SAX J1808.4-3658, Vela X-12 and Her X-1. And then, obtained solutions are concluded.

2. KARMARKAR-TYPE COMPACT STARS MODEL IN f(R,Ø,X) THEORY

Action function of $f(R,\phi,X)$ theory is defined by Tsujikawa (2007).

$$S = \frac{1}{2\kappa}\int d^4x(\sqrt{-g}\, f(R,\phi,X) + S_m \quad (1)$$

Here X denotes kinetic term with $X(\phi) = -\frac{\epsilon}{2}\partial^a\phi\partial_a\phi$. ϵ term indicates canonical ($\epsilon = 1$) or non-canonical ($\epsilon = -1$) scalar fields. For this study, we use $\epsilon = 1$. Field equation $f(R,\phi,X)$ theory is obtained from the least action

$$FG_{ik} - \frac{1}{2}(f - RF)g_{ik} - \nabla_i\nabla_k F - g_{ik}\nabla_a\nabla^a F - \frac{\epsilon}{2}H(\nabla_i\phi)(\nabla_k\phi) = \kappa T_{ik} \quad (2)$$

where f represents $f(R,\phi,X)$ function (Tsujikawa, 2007). Also, $F = \frac{df}{dR}$ and $H = \frac{df}{dX}$. G_{ik} is Einstein tensor known as $G_{ik} = R_{ik} - \frac{1}{2}g_{ik}R$.

For fluid matter, energy-momentum tensor (EMT) is given by

$$T_{ik} = (\rho + p_t)u_i u_k + p_t g_{ik} + (p_r - p_t)\xi_i\xi_k \quad (3)$$

where $u_i\, u^i = -1$ and $\xi_i\xi^i = 1$. u_i and ξ_i represent timelike 4-velocities and spacelike 4-vectors, respectively. We take into account equation of state for radial pressure such as $p_r = \omega\rho$ in the field equations.

By using Riemann tensor and Karmarkar condition, for metric potentials of static spherically symmetric space-time, the relationship between them emerges as $g_{tt} = \left(A + B\int\sqrt{g_{rr} - 1}dr\right)^2$ (Pandey and Sharma, 1982). Spherically symmetric space-time which satisfies Karmarkar condition can be written as follows:

$$ds^2 = (1 + c_0 r^2)dr^2 + r^2 d\theta^2 + r^2 sin^2\theta d\chi^2 - \left(c_1 + \frac{c_2 r^2}{2}\right)^2 c^2 dt^2 \quad (4)$$

where c_0, c_1 and c_2 are constants (Singh *et al.,* 2017). By using Eqs. (2)-(4), field equations of Karmarkar-type anisotropic star model in $f(R,\phi,X)$ theory are obtained as:

$$\frac{1}{8\kappa r(c_0r^2+1)^2(c_2r^2+2c_1)}[-6r(c_0r^2+1)(c_2r^2+2c_1)F'' - 3r\epsilon H(c_2r^2+2c_1)(c_0r^2+1)(\phi')^2 + (14r^4c_0c_2 + (20c_0c_1+8c_2)r^2 + 8c_1)F' + 2r((c_0r^2+1)^2(c_2r^2+2c_1)(\omega-1)\rho + 2(c_0r^2+1)^2(c_2r^2+2c_1)p_t - 2F(r^4c_0^2c_2 + (2c_0^2c_1 - 5c_0c_2)r^2 - 2c_0c_1 - 2c_2))] = \omega\rho \quad (5)$$

$$\frac{1}{4\kappa\, r\,(c_0r^2+1)(c_2r^2+2c_1)}[r(c_0r^2+1)(c_2r^2+2c_1)F'' + \frac{1}{2}r\epsilon\, H(c_2r^2+2c_1)(c_0r^2+1)(\phi')^2 - (r^4c_0c_2 + 6r^2c_0c_1 + 4c_1)F' + r((c_0r^2+1)^2(c_2r^2+2c_1)(\omega-1)\rho + 2(c_0r^2+1)^2(c_2r^2+2c_1)p_t + 2F(r^4c_0^2c_2 + (2c_0^2c_1 + c_0c_2)r^2 + 2c_0c_1 + 2c_2))] = p_t \quad (6)$$

$$\frac{1}{4\kappa(c_0r^2+1)^2(c_2r^2+2c_1)r}[r(c_0r^2+1)c_2r^2 + 2c_1)F'' + \frac{1}{2}r\epsilon H(c_2r^2+2c_1)(c_0r^2+1)(\phi')^2 - (5r^4c_0c_2 - (2c_0c_1 - 4c_2)r^2 - 4c_1)F' + (r((c_0r^2+1)^2(c_2r^2+2c_1)(\omega-1)\rho + 2(c_0r^2+1)^2(c_2r^2+2c_1)p_t + 2F(r^4c_0^2c_2 + (2c_0^2c_1 + 7c_0c_2)r^2 + 6c_0c_1 + 6c_2)))] = -\rho \quad (7)$$

Due to contribution of scalar field in scalar-tensor theories, the nature of matter and field equations are taken into account together with the wave behaviour (Tsujikawa, 2007). So, Klein-Gordon wave equation for $f(R,\phi,X)$ theory can be taken into account as

$$\nabla_i(H\nabla^i\phi) + \epsilon N = 0 \quad (8)$$

where $N = \frac{df}{d\phi}$ (Tsujikawa, 2007). From Eqs. (4) and (8), we get

$$H'\phi' + H[-\frac{\phi' r c_0}{(c_0r^2+1)} + \phi'' + \frac{2\phi'}{r} + \frac{2c_2r\phi'}{(c_2r^2+2c_1)}] + \epsilon\, N\,(c_0r^2+1) = 0 \quad (9)$$

From Eqs. (5)-(9), we achieve solutions of field equations and Klein-Gordon equation for the constructed model in the following forms:

$$\rho(r) = \frac{p_r(r)}{\omega} = \frac{1}{2(\omega+1)(c_2r^2+2c_1)^3(c_0r^2+1)^5}[n\left(c_3c_4r^{(c_4-1)}\right)^{2n}c_5(c_2r^2+2c_1)^3(c_0r^2+1)^{(5-n)} + ((12r^{12}+48r^{10})c_0^4 + (44r^{10}-432r^8)c_0^3 + (60r^8-2592r^6)c_0^2 + (36r^6-1504r^4)c_0 + 8r^4 - 288r^2)c_2^3 + 56c_1\,(\left(r^{10}+\frac{36}{7}r^8\right)c_0^4 + \left(\frac{25}{7}r^8+\frac{132}{7}r^6\right)c_0^3 + \left(\frac{33}{7}r^6-\frac{496}{7}r^4\right)c_0^2 +$$

$$\left(\frac{19}{7}r^4+\frac{40}{7}r^2\right)c_0+\frac{4}{7}r^2+\frac{72}{7})c_2^2+80(\frac{2}{5}+\left(r^8+\frac{36}{5}r^6\right)c_0^4+\left(\frac{17}{5}r^6+\frac{236}{5}r^4\right)c_0^3+\left(\frac{21}{5}r^4-\frac{216}{5}r^2\right)c_0^2+\left(\frac{11}{5}r^2+\frac{32}{5}\right)c_0)c_1^2c_2+32c_0c_1^3((r^6+12r^4)c_0^3+(3r^4+92r^2)c_0^2+(3r^2-32)c_0+1)] \quad (10)$$

$$p_t(r)=\frac{1}{2(\omega+1)(c_2r^2+2c_1)^3(c_0r^2+1)^5}[-n\left(c_3c_4r^{(c_4-1)}\right)^{2n}c_5(c_2r^2+2c_1)^3(c_0r^2+1)^{(5-n)}+2r^2(\omega(c_0r^2+1)((r^{10}-4r^8)c_0^4+(6r^8-4r^6)c_0^3+13r^6c_0^2+(12r^4-32r^2)c_0+4r^2+48)+192+(r^{12}-4r^{10})c_0^5+(r^{10}-32r^8)c_0^4-(3r^8-212r^6)c_0^3-(5r^6-1264r^4)c_0^2-(2r^4-768r^2)c_0)c_2^3+12(\omega(c_0r^2+1)((r^{10}-4r^8)c_0^4+\left(\frac{16}{3}r^8-12r^6\right)c_0^3+\left(\frac{31}{3}r^6+\frac{64}{3}r^4\right)c_0^2+\left(\frac{26}{3}r^4+64r^2\right)c_0+\frac{8}{3}r^2+48)+c_0r^2((r^{10}-4r^8)c_0^4+\left(\frac{5}{3}r^8-40r^6\right)c_0^3-\left(r^6+\frac{236}{3}r^4\right)c_0^2-(3r^4-416r^2)c_0-\frac{8}{3}r^2+\frac{256}{3}))c_1c_2^2+24c_1^2(\omega(\frac{4}{3}+(r^{10}-4r^8)c_0^5+\left(\frac{17}{3}r^8-24r^6\right)c_0^4+\left(\frac{37}{3}r^6-\frac{124}{3}r^4\right)c_0^3+13r^4c_0^2+\left(\frac{20}{3}r^2+\frac{64}{3}\right)c_0)+c_0r^2(-\frac{2}{3}+(r^8-4r^6)c_0^4+\left(\frac{7}{3}r^6-48r^4\right)c_0^3+\left(r^4-\frac{596}{3}r^2\right)c_0^2-(r^2-144)c_0)c_2+16c_0c_1^3(\omega(c_0r^2+1)(2+(r^6-4r^4)c_0^3+4(r^4-7r^2)c_0^2+(5r^2-64)c_0)+c_0r^2(1+(r^6-4r^4)c_0^3+(3r^4-56r^2)c_0^2+(3r^2-276)c_0))] \quad (11)$$

where c_3, c_4 and c_5 are constants related with considered $f(R,\phi,X)$ model. In this study, we assume a hybrid model of $f(R,\phi,X)$ theory. This assumption is an accepted physically meaningful model that allows reducibility to both $f(R)$-class theories and scalar tensor theories (Malik *et. al.,* 2023b). For the hybrid model, $f(R,\phi,X)=f_1(R)+f_2(\phi,X)$ where $f_1(R)=R+\alpha R^2$ (Starobinsky-like $f(R)$-class gravity) and $f_2(\phi,X)=c_5X^n-2V(\phi)$ (Oikonomou and Chatzarakis, 2020). $H(r)$ function in the assumption is obtained as

$$H(r)=-\frac{c_6\,n(\phi')^{2n-2}}{(1+c_0r^2)^{n-1}}. \quad (12)$$

In CS, differences between radial and tangential effects disappear in regions close to core. In accordance with central boundary condition, it is

expected that anisotropy could be disrupted and $p_r|_{r\to 0} = p_t|_{r\to 0}$. It is clearly seen from Eqs. (10) and (11) that Karmarkar-type anisotropic CS in $f(R,\phi,X)$ theory have same radial and tangential pressures at the core:

$$p_r|_{r\to 0} = p_t|_{r\to 0} = -\frac{\omega[(64c_0^2-2c_0)c_1^2-c_1c_2(32c_0+2)-36c_2^2]}{c_1^2\kappa\,(\omega+1)} \quad (13)$$

As can be seen from Eq. (13), $\omega \neq 0$, $\omega \neq -1$ and also $c_1 \neq 0$ must be in order to obtain finite pressure values at the star center accorrding to constructed model. For a CS model investigated in a modified gravity theory, in addition to satisfying center boundary conditions of anisotropic distribution from the solutions obtained, it is also necessary to look at behavior of effective pressures and densities in the center boundary condition. So, from Eq. (2), the effective EMT for $f(R,\phi,X)$ theory is defined as follows:

$$T_{ik}^{eff} = \frac{1}{F}(\kappa T_{ik} + \frac{1}{2}(f-RF)g_{ik} + \nabla_i\nabla_k F - g_{ik}\nabla_a\nabla^a F + \frac{\epsilon}{2}H(\nabla_i\phi)(\nabla_k\phi)) \quad (14)$$

From consideration of Eq. (14) and constructed Karmarkar-type anisotropic CS model, effective energy density, effective radial and tangential pressure are obtained as

$$\rho^{eff} = \frac{c_0(c_0r^2+3)}{\kappa\, c^2(c_0r^2+1)^2} \quad (15)$$

$$P_r^{eff} = \frac{4c_2-c_0c_2r^2-2c_0c_1}{\kappa(c_2r^2+2c_1)(c_0r^2+1)} \quad (16)$$

$$p_t^{eff} = \frac{c_0c_2r^2-2c_0c_1+4c_2}{\kappa(c_0r^2+1)\text{^}2(c_2r^2+2c_1)} \quad (17)$$

From Eqs. (16) and (17), it is seen that pressures of effective matter distributions have finite values at the center of the constructed model such as $p_r^{eff}|_{r\to 0} = p_t^{eff}|_{r\to 0} = \frac{2(2c_2-c_0c_1)}{2\kappa\, c_1}$.

The matching conditions for the continuum of spacetime between interior and exterior regions of a star can be explained as:

$$g_{tt(-)} = g_{tt(+)},\ g_{rr(-)} = g_{rr(+)},\ \frac{\partial g_{tt(-)}}{\partial r} = \frac{\partial g_{tt(+)}}{\partial r}. \quad (18)$$

Exterior region of a star can be defined by Schwarzschild metric.

$$ds^2 = \left(1 - \frac{2GM}{c^2R}\right)^{-1} dr^2 + r^2 d\theta^2 + r^2 sin^2\theta\, d\chi^2 - \left(1 - \frac{2GM}{c^2R}\right) c^2 dt^2 \quad (19)$$

By using the conditions in Eq. (18) and matching the metrics in Eqs. (4) and (19), we obtain c_0, c_1 and c_2 constants.

$$c_0 = \frac{2GM}{R^2(c^2R - 2GM)} \quad (20)$$

$$c_1 = \frac{(5GM - 2c^2R)\sqrt{c^2R^2 - 2GMR}}{2cR(2GM - c^2R)} \quad (21)$$

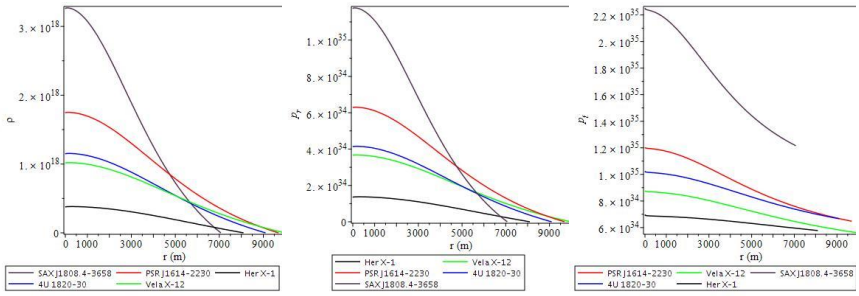
$$c_2 = \frac{GM}{cR^2\sqrt{c^2R^2 - 2GMR}} \quad (22)$$

In order to check physical viability of the obtained solution, we choose to examine the CS listed in Table 1.

Star	M ($M_\odot$)	R (km)	GM / c^2R	References
4U 1820-30	1.58	9.1	0.2559	(Guver *et al.*, 2010)
Her X-1	0.85	8.1	0.1547	(Gangopadhyay *et al.*, 2013)
PSR J 1614-2230	1.97	9.69	0.2997	(Gangopadhyay *et al.*, 2013)
SAX J 1808.4-3658 (SS1)	1.435	7.07	0.2992	(Bhar *et al.*, 2016)
Vela X-12	1.77	9.99	0.2612	(Bhar *et al.*, 2016)

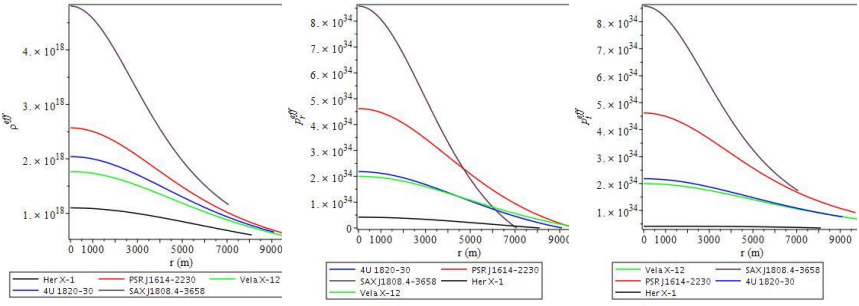
Table 1. Mass and radius data of CS.

In this study, for effective matter distribution, we choose integration constants as $c_3 = 35.5733732987$ $c_4 = -1$, $c_6 = -c^2$ and assume $n = 2$ in Eq. (12). For normal matter distribution, we assume $n = 0.001$, $c_3 = c_4 = -1$ and $c_5 = -0.23883\ 10^{-4}$ for PSR J1614-2230, $c_5 = -0.25365\ 10^{-4}$ for 4U 1820-30, $c_5 = -0.4478288\ 10^{-4}$ for SAX J1808.4-3658, $c_5 = -0.212579884\ 10^{-4}$ for Vela X-12, $c_5 = -0.2329976\ 10^{-4}$ for Her X-1. Also, we take that $\omega = 0.4$.



(a) (b) (c)

Fig. 1. Graph of a) energy density b) radial pressure c) tangential pressure for normal matter distribution with respect to radius in unit of kg/m³.



(a) (b) (c)

Fig. 2. Graph of a) effective energy density b) effective radial pressure c) effective tangential pressure with respect to radius in unit of kg/m³.

Mass function of a stellar object can be written as follows.

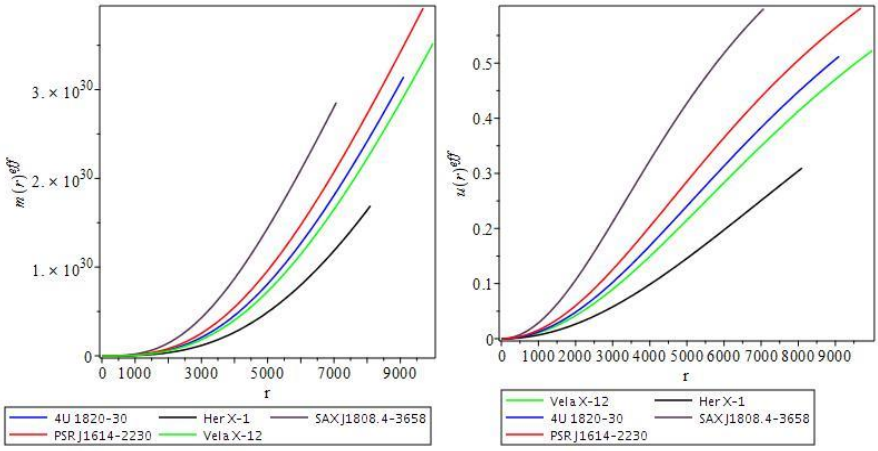
$$m(r) = \int_0^r 4\pi r^2 \rho(r) dr \quad (23)$$

Eq. (23) gives total mass of the star at $r = R$ such as $m(R) = M$.

The compactness factor is given by

$$u(r) = \frac{2m(r)}{r} \quad (24)$$

In this work, we compare compactness factor with Buchdahl limit $\frac{2GM}{c^2R} \leq \frac{8}{9}$.



(a) (b)

Fig. 3. a) Graph of mass function b) graph of compactness factor for effective matter distribution.

Surface redshift of a star is shown as

$$z = \frac{1}{c_1 + \frac{c_2 r^2}{2}} - 1 \quad (25)$$

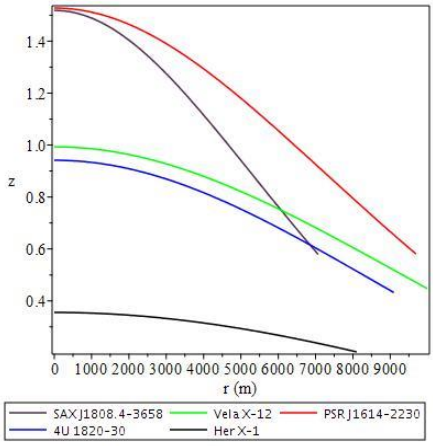


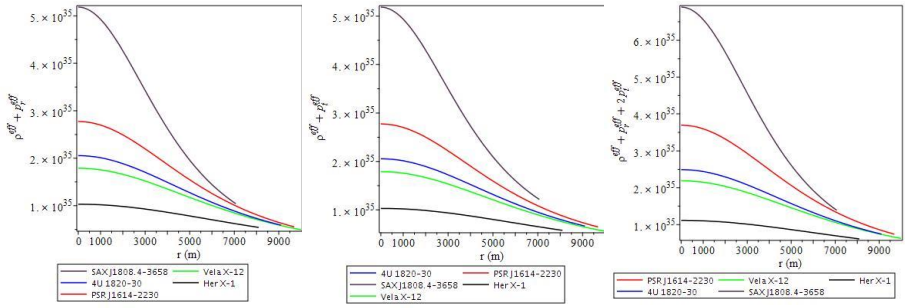
Fig. 4. Graph of redshift function with respect to radius.

Weak energy condition (WEC) ensures positive matter density for all observers. WEC for anisotropic fluid can be written down as follows.

$$\rho^{eff} \geq 0,\ \rho^{eff} + p_r^{eff} \geq 0,\quad \rho^{eff} + p_t^{eff} \geq 0. \tag{26}$$

Strong energy condition (SEC) implies attractive gravity. SEC is given by

$$\rho^{eff} + p_r^{eff} + 2p_t^{eff} \geq 0 \tag{27}$$



(a) (b) (c)

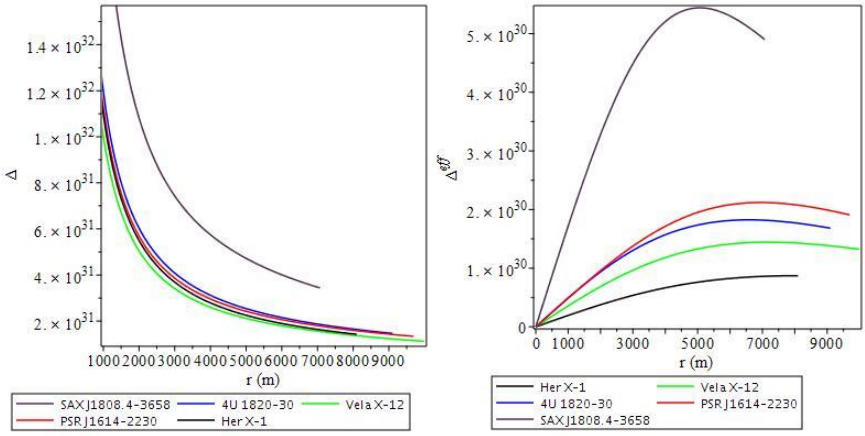
Fig. 5. Graph of a)WEC for P_r^{eff} b)WEC for P_t^{eff} c) SEC with respect to radius.

Energy conditions, depicted in Fig. 5, are satisfied for all selected CS.

We use anisotropic fluid as matter form. Therefore, it would be useful to investigate anisotropy parameter. Anisotropy parameter is defined by

$$\Delta = \frac{2}{r}(P_t - P_r) \tag{28}$$

Anisotropy parameter in Eq. (28) plotted in Fig. 6 for normal and effective pressures.



(a) (b)

Fig. 6. Graph of anisotropy parameter for a) normal matter distribution b) effective matter distribution.

Causality condition requires that sound speed in any matter form does not exceed the speed of the light. Sound speed for radial pressure is

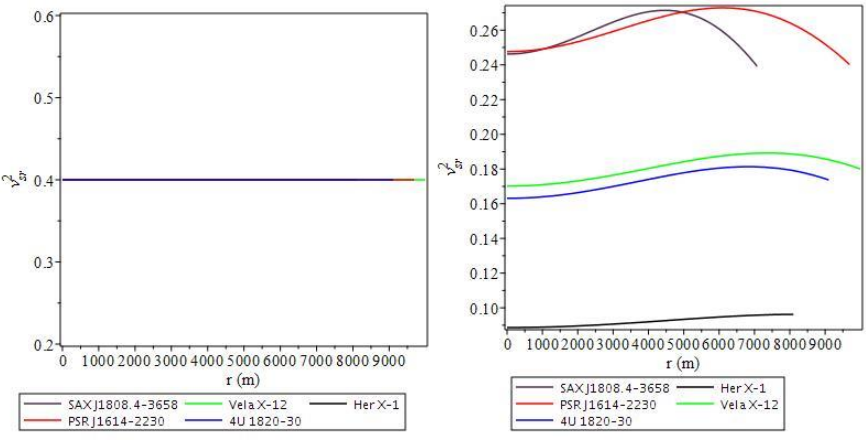
$$\upsilon_{sr}^2 = \frac{dP_r}{c^2 d\rho}\,.$$

(29)

Sound speed for tangential pressure can be written as follows.

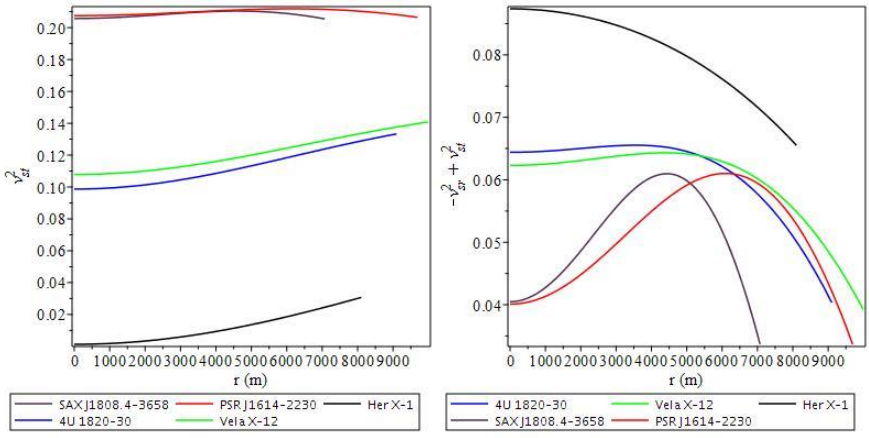
$$\upsilon_{st}^2 = \frac{dP_t}{c^2 d\rho}$$

(30)



(a) (b)

Fig. 7. Graph of sound speed of radial pressure for a) normal matter distribution b) effective matter distribution.



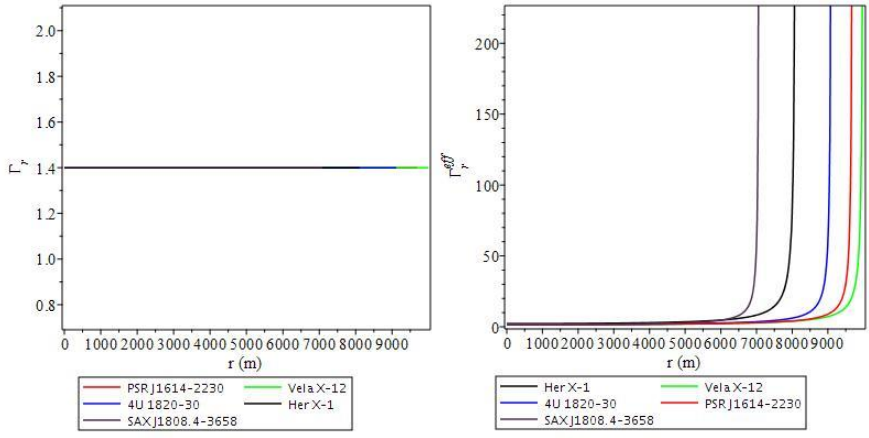
(a) (b)

Fig. 8. a) Graph of sound speed of tangential pressure for effective matter distribution b) graph of $\upsilon_{st}^2 - \upsilon_{sr}^2$ for effective matter distribution.

Adiabatic index is given by

$$\Gamma_r = \frac{c^2\rho + p_r}{p_r}\frac{dp_r}{c^2 d\rho} \quad (31)$$

For stable stellar structure, adiabatic index must be $\Gamma_r \geq 4/3$.



(a) (b)

Fig. 9. Graph of adiabatic index for a) normal matter distribution b) effective matter distribution.

Tolman-Oppenheimer-Volkoff (TOV) equation is taken to account to examine hydrostatic equilibrium of a star. By using conservation of effective EMT, $\nabla^i T_{ik}^{eff} = 0$, components of TOV equation are obtained as follows.

Effective gravitational force is given by

$$F_g^{eff} = \frac{2c_2 r}{c_2 r^2 + 2c_1}\left(c^2 \rho^{eff} + P_r^{eff}\right) \tag{32}$$

Effective hydrostatic force is

$$F_h^{eff} = \frac{dP_r^{eff}}{dr} \tag{33}$$

Effective anisotropic force can be shown as

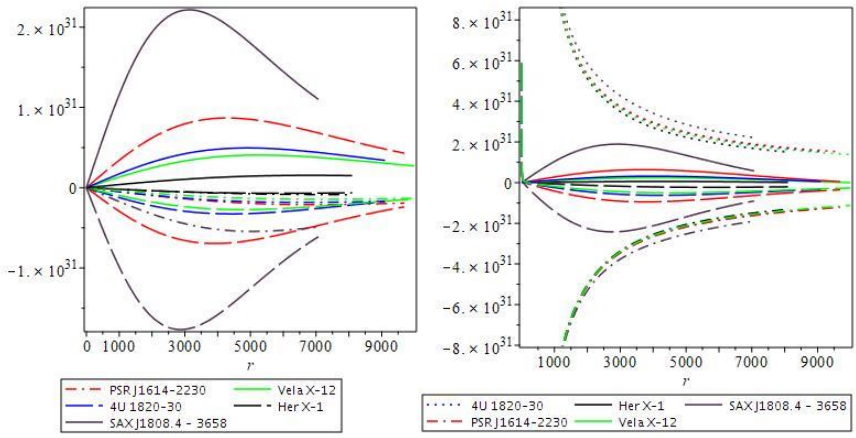
$$F_a^{eff} = -\frac{2}{r}\left(P_t^{eff} - P_r^{eff}\right) \tag{34}$$

Effective gravitational, hydrostatic, anisotropic forces satisfy following condition.

$$F_g^{eff} + F_h^{eff} + F_a^{eff} = 0 \tag{35}$$

On the other hand, for normal matter distribution, normal counterparts of Eqs. (32) - (35) is taken into account. TOV equation has an extra force F_e in Eq. (35) due to $f(R, \phi, X)$ theory contribution.

$$F_e = \frac{2c_2 r}{c_2 r^2 + 2c_1}\left(\left(c^2 \frac{c_0(c_0 r^2 + 3)}{\kappa c^2 (c_0 r^2 + 1)^2} - c^2 \rho(r)\right) - \left(\frac{c_0 c_2 r^2 + 2c_0 c_1 - 4c_2}{\kappa(c_0 r^2 + 1)} + p_r(r)\right)\right) - \frac{d}{dr}\left(\frac{c_0 c_2 r^2 + 2c_0 c_1 - 4c_2}{\kappa(c_0 r^2 + 1)} + p_r(r)\right) - \frac{2}{r}\left(\left(\frac{c_0 c_2 r^2 - 2c_0 c_1 + 4c_2}{\kappa(c_0 r^2 + 1)^2 (c_2 r^2 + 2c_1)} + \frac{c_0 c_2 r^2 + 2c_0 c_1 - 4c_2}{\kappa(c_0 r^2 + 1)}\right) - \left(p_t(r) - p_r(r)\right)\right) \tag{36}$$



(a) (b)

Fig. 10. a) Graph of F_g^{eff} (solid), F_h^{eff} (dashed) and F_a^{eff} (dash-dot) for effective matter distribution b) Graph of F_g (solid), F_h (dashed), F_a (dash-dot) and F_e (dot) for normal matter distribution.

3. CONCLUSION

In this paper, we have investigated anisotropic CS by using spherically symmetric spacetime satisfying Karmarkar condition in $f(R,\phi,X)$ theory. We have obtained normal and effective matter distribution of anisotropic fluid.

In order to examine physical viability of obtained solutions, we use observational data of CS PSR J1614-2230, 4U 1820-30, SAX J1808.4-3658, Vela X-12 and Her X-1. Our findings can be summarized as follows.

a) Effective and normal radial pressure vanishes at the surface of CS with suitable choice of arbitrary integration constants. Also, it is obtained equal radial and tangential pressure ($P_r = P_t$ and $P_r^{eff} = P_t^{eff}$) as expected at the center of the star.

b) Energy conditions (SEC and WEC) are met. This means positive matter density (WEC) and attractive gravity (SEC) for all observers. In the CS case, these results ensure physically acceptable matter distribution.

c) Sound speed for radial direction fulfills $0 \leq v_{sr}^2 \leq 1$ condition for normal and effective matter distributions.

d) Compactness factor is satisfied Buchdal limit condition such as $\frac{2MG}{c^2R} \leq \frac{8}{9}$ for all selected CS.

e) TOV equation is depicted for effective and normal matter distributions in Fig. 10. Hydrostatic equilibrium conditions are met for both cases.

f) As it can be see in Fig. 6, anisotropy parameter for both normal and effective matter distribution is positive for selected CS. That means anisotropy is directed outward. Malik *et al.* (2023b) discussed validity of the model and $f(R, \phi, X)$ theory using data from LCM X-4, Cen X-3, EXO 1785-248. The authors obtained anisotropy parameter for normal matter as increasing with radius in all three stars. Data for stars considered in our study, the anisotropy parameter of the normal matter distribution of our proposed model decreases with radius. On the other hand, it has been observed that this parameter gives increasing results for the distribution of the effective matter.

g) Mass-radius function, redshift function, adiabatic index are also investigated. We use linear EoS $p_r = \omega_r \rho$ where $\omega_r = \Gamma_r - 1$. Therefore, adiabatic index (Γ_r) depends on the choice of ω_r parameter.

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CHAPTER 4

INVESTIGATION OF THE INTERACTIONS OF THE SYNTHESIZED PYRIMIDINE DERIVATIVE WITH DIFFERENT TARGETS BY USING IN SILICO APPROACHES

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1. Introduction

Pyrimidine, a nitrogen-containing six-membered heterocycle, and its derivatives have antibacterial, antimicrobial, antiallergic, antitumor, antiviral, tuberculostatic, antifolate, antileishmanial, calcium channel antagonist, antifungal anti-inflammatory, analgesic, diuretic, anticonvulsant, and tyrosine kinase activities (Figure 1) (Brown, 2018; Butters et al., 2001; De Clercq, 2004; Katritzky & Lagowski, 2013). They play important roles in biological processes carried out by many compounds such as coenzymes, vitamins, nucleotides, purines, pterines, and nucleic acids. Pyrimidine incorporated compounds are a research area of great importance in synthetic and heterocyclic chemistry due to their sui generis structure that has diverse applications in many fields of pharmaceutical, agricultural, and material sciences. Therefore, the synthesis of pyrimidine-based molecules plays important roles for biodynamic heterosystems.

The properties of pyrimidines are predominantly controlled by two nitrogen atoms' electron-withdrawing properties. Their presence in nucleobases in DNA and RNA allows pyrimidines to directly participate in the coding of genetic information, controlling protein synthesis and amino acid sequence.

It is known that designing novel molecular structures of potential drugs with various therapeutic activities is very attractive and useful. Designing efficient chemical reaction sequences with high complexity and structural variety, providing molecules with antidivorce bioactivities, is still of great importance in organic chemistry (Figure 1) (Abu-Hashem, El-Shehry, & Badria, 2010; Amir, Javed, & Kumar, 2007; Basavaraja, Sreenivasa, & Jayachandran, 2005; Dea-Ayuela et al., 2009; Juby, Hudyma, Brown, Essery, & Partyka, 1979; Kappe, 1993; Kumar, Khan, Tekwani, Ponnan, & Rawat, 2015; Ram, Haque, & Guru, 1992; Smith & Kan, 1964).

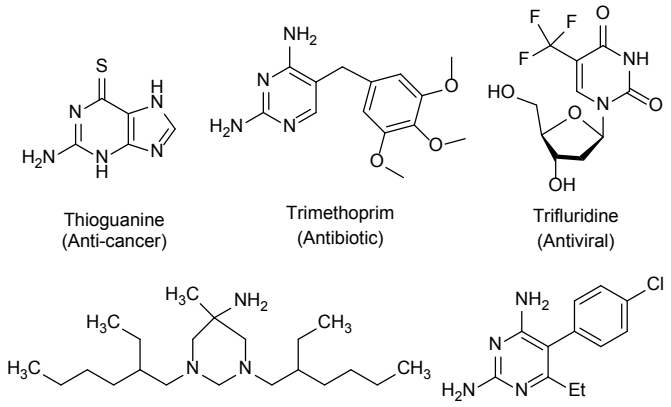
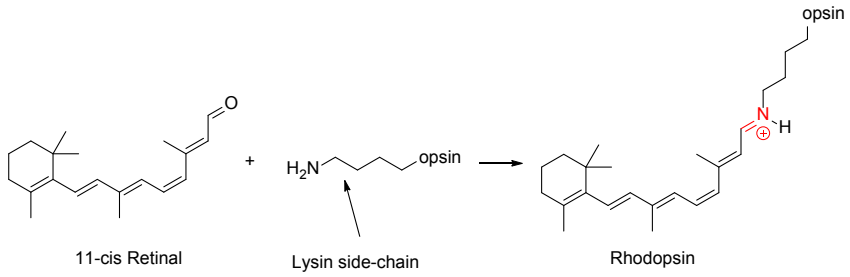


Figure 1. *Some pyrimidine-bearing bioactive molecules*

Schiff bases, also named as imine or azomethine, have been known since Hugo Schiff's synthesis by condensation reaction of carbonyl compounds (aldehyde or ketone) with primary amines in 1884 (Dea-Ayuela et al., 2009). Recently, investigation on Schiff bases and their organometallic compounds has expanded a lot. The significance of Schiff base and its complexes for organic and inorganic chemistry, catalysis, biomedical applications, and materials science etc. is well explored and studied (Majumdar & Chattopadhyay, 2011).

Recently, broad spectrum of bioactivities of Schiff bases have been investigating by many researchers. It is reported that some Shiff base-bearing compounds have various biological activities such as anti-inflammatory, antiviral, antibacterial, antimicrobial, antifungal, antitumor, and herbicidal (Amer, El-Wakiel, & El-Ghamry, 2013; Bensaber et al., 2014; Güngör & Gürkan, 2014; Pontiki, Hadjipavlou-Litina, & Chaviara, 2008; Shanty et al., 2017).

An imine bond between protein opsin and 11-cis retinal which is derived from retinol (vitamin A) in retina of the eye demonstrate crucial role in the chemistry of vision. The reaction generates a light-sensitive receptor protein, rhodopsin, which is the opsin of rod cells in the retina and is triggers visual phototransduction in the rods (Scheme 1).



Scheme 1. *Synthesis scheme of rhodopsin by an imine linkage*

It is still important to synthesize and examine the bioactivity of pyrimidine and Schiff base derivatives since they demonstrate have various biological activities (Eliot & Kirsch, 2004; Hernandez-Molina & Mederos, 2004) . At his context, in this study, a novel pyrimidine and Schiff base bearing compound synthesized, and its enzyme interactions examined *in silico* by molecular docking.

At first, via reaction of furan-2,3-dion and semicarbazon in benzene, amino pyrimidine (Z1) as reagent was synthesized. And then, pyrimidine and Schiff baze bearing molecule (**Z2**) was synthesized by the reaction of 2-bromobenzaldehyde and compound (**Z1)** under reflux conditions (Scheme 2). Molecular structure of compound (**Z2)** was characterized by ^{1}H-NMR, ^{13}C-NMR, and FTIR spectra.

The compound (**Z2)** was synthesized and examined, and its interactions with theoretically determined targets were calculated by *in silico* approaches. The aim here is to computationally determine the interactions of compound (**Z2)** in different diseases, which will guide future studies. Epidermal growth factor receptor (EGFR), estrogen receptor (ER) and acetylcholinesterase (AChE) enzyme are targets for molecular docking in this study. The result of the *in silico* approaches in this study is also remarkable, as theoretical calculations are now considered both a preliminary study and a complement to experimental data.

2. Materials and Method

2.1. Experimental

All solvents and reagents were bought commercial companies like sigma-aldrich, merck, alfa easer and used without further purification. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker 400 MHz Ultra Shield instrument. Melting point was determined by digital melting point apparatus (Electrothermal 9100). By using Camag TLC lamp (254/366 nm) and TLC 60 F254 (Merck), the reaction medium checked routinely. IR spectrum was recorded on a Shimadzu Model 8400 FT-IR spectrophotometer.

2.2. Synthesis of Schiff Base

2.2.1. (*E*)-1-(2-Bromobenzylideneamino)-5-(4-methoxybenzoyl)-4-(4-methoxyphenyl) pyrimidin-2(1*H*)-one (Z2)

1 mmol (**Z1**) and 1.2 mmol 2-bromobenzaldehyde were taken in a reaction flask and 20 mL of ethyl alcohol was added as solvent and *p*-toluene sulfonic acid (PTSA) as catalyst. Then the mixture had been refluxed for 11 hours. After 11 hours, ethanol was evaporated by rotavapor. To solve viscose residue, diethyl ether had been added and stirred for 12 hours. The precipitation was filtered and recrystallized by ethyl alcohol. The reaction was regularly controlled by TLC. The structure of (**Z2**) was determined by using analytical and spectroscopic methods. Yield: (55%); m.p.: 201-202 ^{o}C; color: yellow. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) = 9.78 (s, 1H, N=CH), 8.55 (s, 1H, CH in pyrim.), 7.96-6.95 (m, 12H, Ar-H), 3.79 (d, 6H, 2CH_3O-). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) = 190.74, 169.89, 164.02, 163.57, 162.05, 151.84, 149.07, 134.73, 134.04, 132.81, 131.78, 131.22, 129.95, 129.18, 128.91, 128.82, 125.97, 116.29, 114.51, 114.27, 56.11, 55.82. FT-IR: υ = 3053.2 (arom. C-H), 2991.4 (aliph. C-H), 1677.3, 1645.3 (C=O), 1598.0 (C=N), 1572.1 (C=C). Molecular Formula: $C_{26}H_{20}N_3O_4$ and Formula Weight: (438 g/mol).

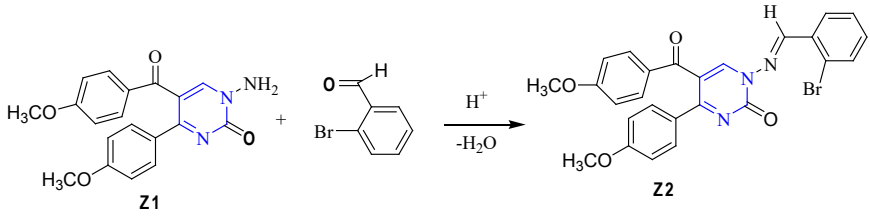
2.3. Molecular Docking

Schrödinger 2021-2 Glide program was used in the calculations of in silico approaches (Schrödinger Release 2021-2: Glide). . The protocol applied in molecular docking studies is the same as in the method section of previous studies (BozbeyMerde, Önel, Türkmenoğlu, Gürsoy, & Dilek, 2022; Merde et al., 2022; TÜRKMENOĞLU, 2022a, 2022b). Crystal structures of the identified targets were downloaded from the protein database. Compound (**Z2**) was optimized and prepared in the LigPrep wizard (https://www.rcsb.org/) of the program (Schrödinger Release 2021-2: LigPrep). OPLS2005 force field, which is used in molecular docking methods, was used. Free binding energy was calculated by applying the MM-GBSA method.

3. Results and Discussion

3.1. Experimental

The compound (**Z1)** was prepared from the furan-2,3-dione derivative using the method specified in the literature. A new Schiff base (**Z2**) was synthesized by the condensation of compound (**Z1**) with 2-bromobenzaldehyde at 65% (Scheme 1). The compound was purified by recrystallization. Synthesis of Schiff bases are usually carried out by reactions of amines with carbonyl compounds by addition and subtraction. In the IR spectrum of Schiff bases, characteristic stretch bands of carbonyl (C=O) groups are observed. In the ^{1}H NMR spectra of the compounds, the striking peak belongs to the azomethine proton.



Scheme 2. *A synthesis scheme of compound (***Z2***)***.**

In the IR spectrum of compound (**Z2**), the two C=O absorption bands were observed at 1677.3 and 1645.3 cm^{-1}. In the ^{1}H NMR spectrum, the N=CH proton was resonated in the downfield area at δ 9.78 ppm. The proton signal for -CH in the pyrimidine ring for (**Z2)** was detected singlet at δ 8.55 ppm. Aromatic protons were observed as multiplet between δ 7.96 and 6.75 ppm. Also, methoxy protons were observed dublet at 3.79 ppm. In the ^{13}C NMR spectrum, benzoyl carbon's signal was observed at δ 190.74 ppm. The signals of CH_3O- groups were observed at 56.11, 55.82 ppm as

singlets. Other carbons of the molecule were obtained between δ 169.89-114.27 ppm. The data obtained because of the analyses fully confirmed the structure of Schiff base.

3.2. Molecular Docking

Molecular docking studies of compound **(Z2)** were performed to support the synthesis study. The purpose of this is to lead the way for subsequent studies. Studies on cancer and Alzheimer's were conducted with *in silico* approaches. For this purpose, three different targets were chosen. Compound (**Z2**) interacted in silico with EGFR, ER and AChE targets. The most striking computational results are the *in silico* calculations made against Alzheimer's disease.

Since three different diseases were examined in molecular docking, three different crystal structures were selected from the protein database. The crystal structures of 4HJO (Park, Liu, Lemmon, & Radhakrishnan, 2012) for EGFR, 3ERT(Shiau et al., 1998) for ER and 4EY7 (Cheung et al., 2012) for AChE were analyzed. The results of the interactions of compound (**Z2)** of each crystal structure with *in silico* approaches are presented in Table 1.

Table 1. *Parameter values of the interactions of compound (***Z2***) with 4HJO, 3ERT and 4EY7 crystal structures via in silico approaches.*

PDB ID	Compound	Docking Score	Glide Gscore	Glide Energy	ΔG_{Bind}
4HJO	**Compound (Z2)**	-7.094	-7.094	-53.206	-63.42
	Erlotinib	-9.608	-9.608	-56.809	-89.81
3ERT	**Compound (Z2)**	-7.235	-7.235	-42.589	-51.25
	Tamoxifen	-11.304	-11.324	-54.896	-81.68
4EY7	**Compound (Z2)**	-10.811	-10.811	-53.725	-71.87
	Tacrine	-10.450	-10.450	-31.620	-53.88

The parameter values of the compound **(Z2)** in Table 1 are compared with the reference compounds for each target and are presented in Table 1. The purpose of this is to determine whether these values, which are examined only computationally, will be supportive for future studies. Erlotinib was used as reference for EGFR target, Tamoxifen was used as reference for ER target, and Tacrine was used as reference for AChE. When the first target EGFR in Table 1 is examined, the Docking Score, Glide Gscore, Glide Energy, ΔG_{Bind} of compound (**Z2)** are -7.094, -7.094, -53.206, -63.42 kcal/mol, respectively. When these values were compared with the reference compound Erlotinib, it was determined that the docking score values were close to each other.

The 2D and 3D interaction diagrams of the EGFR-Compound **(Z2)** complex, whose binding parameter values are presented in Table 1, are presented in Figure 3. In Figure 3, it is understood that compound **(Z2)** makes hydrogen bonds with amino acid Cys773 and amino acid Met769 and docked in the active binding site of the target.

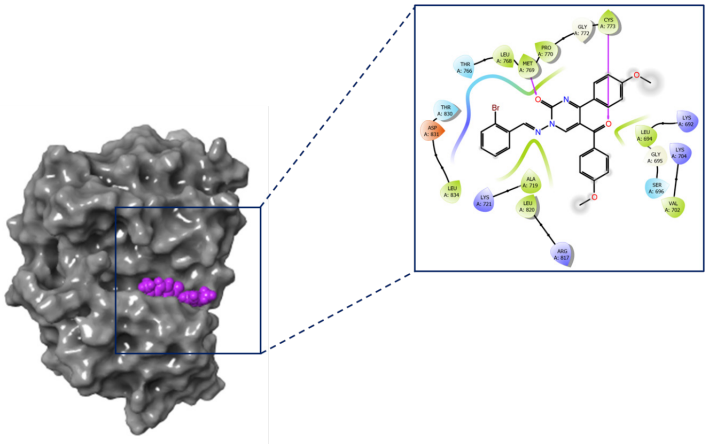


Figure 3. *2D and 3D diagram of the interaction of compound (***Z2***) with the 4HJO crystal structure.*

The binding parameter values of the estrogen receptor determined as the second target are presented in Table 1 for both compound **(Z2)** and Tamoxifen. The docking score value of compound Z**(2)**, which interacts with the 3ERT crystal structure in Table 1, is -7235 kcal/mol, while the free binding energy value is -5125 kcal/mol. Binding parameter values of tamoxifen were also calculated closely. Additionally, the 2D and 3D interaction diagram of the ER-compound **(Z2)** complex is presented in Figure 4. It was determined that compound **(Z2)** approaching from the binding region of the 3ERT crystal structure makes hydrogen bond with the Cys530 amino acid residue.

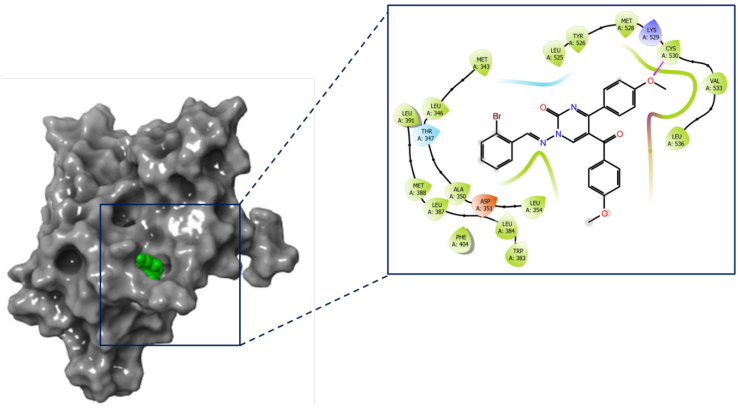


Figure 4. *2D and 3D diagram of the interaction of compound (***Z2***) with the 3ERT crystal structure.*

Undoubtedly, the most striking of the theoretically determined targets was AChE. It has guided both us and the researchers who will work on this subject. The reason for this is the binding parameter values presented in Table 1 because of the interaction of compound (**Z2**) with AChE. In Table 1, the docking score value of the AChE-compound (**Z2**) complex is -10.811 kcal/mol. The binding parameter value of the AChE-Tacrine complex presented in Table 1 is calculated to be lower, that is, -10.450 kcal/mol. In Table 1, not only the docking score value but also the Glide gscore and Glide energy value of the compound (**Z2**) interacting with AChE were determined to be better. When the free binding energy values, which are indicators of the interaction between ligand and target, are examined in Table 1, AChE-Compound (**Z2**) is -71.87 kcal/mol, while AChE-Tacrine complex is -53.88 kcal/mol.

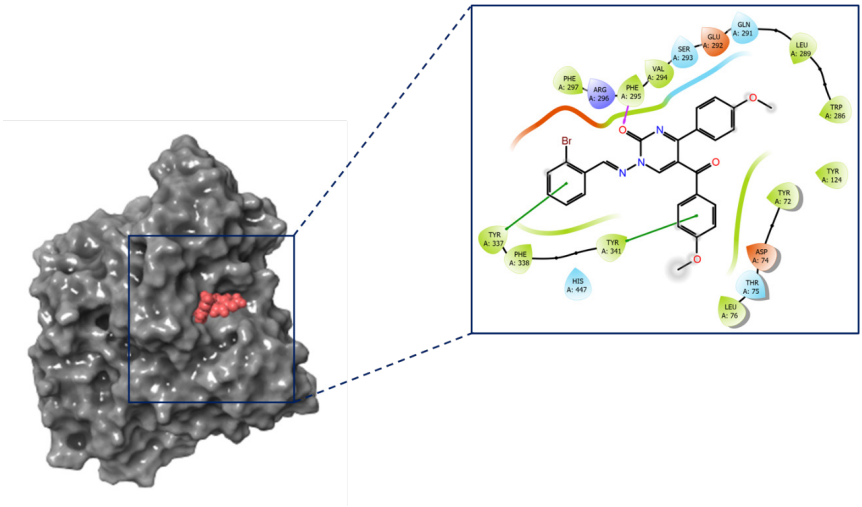


Figure 5. *2D and 3D diagram of the interaction of compound (***Z2***) with the 4EY7 crystal structure.*

When these binding parameter values are analyzed for all three targets, it can be clearly stated that all three have good results, but the AChE target has the best binding parameter values. Additionally, in Figure 5, it is shown that the compound **(Z2)** is docked in the active pocket region in both the 3D diagram. Additionally, in the 2D interaction diagram, it was determined that it interacts with amino acids that are important for the inhibition of AChE. In Figure 5, it was determined that compound (**Z2**) made a hydrogen bond with the Phe295 amino acid residue and an π-π bond with the Tyr337 amino acid residue. This may be the reason why bonding parameter values are calculated better.

CONCLUSION

In this study, a new pyrimidin-2(1H)-one derivative (**Z2**) was synthesized and examined with in silico approaches. The structure of the synthesized compound (**Z2**) was determined experimentally, and its interaction was examined using in silico approaches. The results of the interaction of the synthesized compound (**Z2**) with the theoretically determined targets in molecular docking studies are quite remarkable. The results of the compound **(Z2),** which interacted with ER, EGFR and AChE in silico, were determined to be instructive when compared with the references. It has been determined that especially for AChE, compounds **(Z2)** and derivatives of (**Z2**) can be examined *in vitro*.

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CHAPTER 5

BIOLOGICAL ACTIVITIES, AREAS OF USE, NUTRITIONAL AND MINERAL CONTENTS OF PURSLANE (*PORTULACA OLERACEA*)

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Introduction

Medicinal plants have been one of the most important natural resources of humankind since prehistoric times (Mohammed et al., 2022). Their nutritional properties have placed plants at the top of diet lists. Plants, which contain many nutritious vitamins, minerals and nutrients, are used for different purposes (Mohammed et al., 2020a; Korkmaz et al., 2021). The potential medicinal uses of plants have been very beneficial to humans (Sevindik et al., 2017). In this context, these plants, called medicinal plants, are used to combat different diseases (Mohammed et al., 2020b). Many studies have reported that plants have many biological activities such as anticancer, antimicrobial, antiproliferative, antioxidant, hepatoprotective, and DNA protective (Mohammed et al., 2018; Mohammed et al., 2019; Mohammed et al., 2021b; Comlekcioglu et al., 2022; Unal et al., 2022; Kalkan et al., 2023; Uysal et al., 2023). In this context, it is important to reveal the biological activities of plants in order to determine their medicinal potential (Pehlivan et al., 2018; Mohammed et al., 2023a). In this study, the biological activities of Portulaca oleracea L. reported in the literature were compiled. Additionally, usage areas, mineral and nutritional contents have been compiled.

Portulaca oleracea (Portulacaceae) is a herbaceous wild plant. It is thought that the name Portulaca is derived from the Latin 'porto'. Additionally, the expression 'lac' comes from the meaning of milk because the plant contains a milky sap. It grows wild in other hot countries (Mediterranean countries, Africa, Asia, etc.) such as America, India, Spain, Mexico, New Zealand, France, Venezuela, Australia, Turkey and India. It is a species with a very wide distribution area in terms of ecosystem. When we look at the morphological structure of purslane, the first thing that attracts attention is that it has a thick and fleshy leaf at the top that stores water. Its leaves are usually stemless and 6.25 mm in size. Several flowers are located together in stemless terminal heads. The color formation in the stemmed ones is generally red. The plant is 15-30 cm tall (Chowdhary et al., 2013; Syed et al., 2016; Kumar et al., 2021; Srivastava et al., 2021; Aini et al., 2022).

Usage Areas

When we look at the literature research in terms of the usage areas of purslane, it is noteworthy that it is primarily for nutritional and therapeutic purposes. Purslane burns, sexual desire, bladder disorders, headaches, intestinal diseases, worm disease, dysentery, liver disease, stomach disease, cough, shortness of breath, arthritis, inflammation of the eyes and other organs, dental disease, gingivitis, kidney disease. It is used in conditions such as discomfort, urogenital disorder, skin disorder, meningitis, encep-

halitis, thirst, melancholy, sore throat, earache, cholesterol, hoarseness, cardiovascular disease, dysmenorrhea, sinusitis, muscle pain, insect bite, asthma, oral sores, hemorrhoids. is known. It has also been reported that it is used in salads, pies, soups, omelets, dairy products, meat products and other consumed foods (Guarrera, 2003; Simopoulos, 2004; Megaloudi, 2005; Lans, 2006; González-Tejero et al., 2008; Bosi et al., 2009; Carrió and Vallès, 2012; Guarrera and Savo, 2013; Sultana and Rahman, 2013; Khanam et al., 2019).

Nutritional and Mineral Contents

Plants are important natural products that stand out with their nutritional properties. In this study, the mineral and nutritional contents of *P. oleracea* were compiled according to the data reported in the literature. The findings obtained are shown in table 1.

Table 1. Nutritional and Mineral Contents of Portulaca oleracea

Nutritional Composition	Values (%)
Protein	7.53-44.35
Carbohydrate	1.2-62.47
Lipid	0.68-1.63
Ash	3.00-27.3
Mouisture	0.80-93.5
Crude fibre	13.34-20.3
Mineral Composition	**Values (mg/100g)**
P	2.99-360
K	19.34-6920
Na	0.52-85.66
Fe	0.18-14.05
Ca	4.54-900
Mg	4.95-300

Protein (7.53-44.35%), carbohydrate (1.2-62.47%), lipid (0.68-1.63%), ash (3.00-27.3%), mouisture (0.80-93.5%) and crude fiber (13.34-20.3%) values of *P. oleracea* have been reported in the literature (Mohamed and Hussein, 1994; Obied et al., 2003; Turan et al., 2003; Ezeabara et al., 2014; Alu'datt et al., 2019). Additionally, P (2.99-360 mg/100g), K (19.34-6920 mg/100g), Na (0.52-85.66 mg/100g), Fe (0.18-14.05 mg/100g), Ca (4.54-900 mg/100g) and Mg (4.95-300 mg/100g) values have been reported (Mohamed and Hussein, 1994; Obied et al., 2003; Turan et al., 2003; Ezeabara et al., 2014; Santiago-Saenz et al., 2018).

Biological activities

Plants synthesize hundreds of chemical compounds for various functions, including defense and protection against different living organisms in the ecosystem, such as insects, fungi and herbivorous mammals. It is known that plants have biological activities thanks to these chemical compounds (Akgül et al., 2020; Mohammed et al., 2023c; Sevindik et al., 2023). In this context, in this study, the biological activities of *P. oleracea* reported in the literature were compiled. According to the findings, it was observed that extracts such as oil extract, methanol, ethanol, water, alcoholic, water-methanolic, hydroalcoholic, chloroform, petroleum ether, ethyl acetate, acetone and hexane were used in in vitro and in vivo studies. Biological activity studies of Portulaca oleracea reported in the literature are shown in table 2.

Table 1. Biological activity of Portulaca oleracea

Biological activities	Extraction	Geographic regions	References
Antioxidant, antimicrobial, cytotoxic, anticancer, hepatoprotective, anti-aging, anti-inflammatory, antileishmanial, anti-melanogenesis, anti-photoaging, antispasmodic, antiulcerogenic, antiviral, antihyperlipidemic, antihelmıntıc, herbicidal, antitumor	Oil extract, methanol, ethanol, water, alcoholic, water-methanolic, hydroalcoholic, chloroform, petroleum ether, ethyl acetate, acetone, hexane	Turkey, China, Ethiopia, Malaysia, Spain, Tunusia, Iran, Portugal, Italy, Egypt, South Korea, India, Philippines, Saudi Arabia	(Bae, 2004; Karimi et al., 2004; Lim and Quah, 2007; Cho et al., 2008; Zhang et al., 2009; Chen et al., 2010; Anusha et al., 2011; Londonkar and Nayaka, 2011; Erkan, 2012; Uddin et al., 2012; Yan et al., 2012; Silva and Carvalho, 2014; Tian et al., 2014; Wasnik and Tumane, 2014; Jalali Mousavi et al., 2015; Mousavi et al., 2015; Taha and Osman, 2015; Eskandari et al., 2016; Sallam and Anwar, 2017; Zhao et al., 2017; Catap et al., 2018; Jin et al., 2018; Kim et al., 2018; Nazeam et al., 2018; Sicari et al., 2018; Li et al., 2019; Yang et al., 2019; Xiu et al., 2019; Dabbou et al., 2020; Desta et al., 2020; Saffaryazdi et al., 2020; Khursheed and Jain, 2021; Fernández-Poyatos et al., 2021; Alipour et al., 2022; Fouda et al., 2022; Tao et al., 2023)

Antioxidant activity

Reactive oxygen species are oxidant compounds produced as a result of metabolic activities in living organisms (Krupodorova and Sevindik, 2020). While low levels of these compounds are not harmful to living things, as levels rise they can cause serious cellular damage. As the levels of oxidant compounds increase, the antioxidant defense system comes into play and suppresses them (Bal et al., 2019; Gürgen and Sevindik, 2022). However, as the levels of oxidant compounds become too high, the antioxidant defense system becomes inadequate. In this case, oxidative stress occurs (Eraslan et al., 2021). As a result of oxidative stress, serious diseases such as cancer, cardiological disorders, Alzheimer's, Parkinson's, and multiple sclerosis may occur (Selamoglu et al., 2020; Saridogan et al., 2021; Bal et al., 2023). Supplementary antioxidants may serve to reduce the effects of oxidative stress. Plants are important natural sources of antioxidant supplements (Akgül et al., 2022). In this study, antioxidant activity studies of Portulaca oleracea reported in the literature were compiled. In a study conducted in Turkey, the antioxidant status of the fractions obtained from the crude extract of *P. oleracea* by reverse phase separation method was investigated. As a result of the study, it was reported that the LC50 value range of the fractions was 154.1- 1014.2 µg/mL (Erkan, 2012). In a study conducted in China, the antioxidant status of homoisoflavone obtained from *P. oleracea* was investigated using the DPPH test. As a result of the research, it was reported that the DPPH LC50 value was 17.78 Mm (Yang et al., 2019). In a study conducted in Ethiopia, the antioxidant status was investigated using the DPPH test from the oil extract obtained from the seeds, leaves and stems of *P. oleracea*. As a result of the review, it was reported that the highest DPPH percentage was 12.55% from the extract obtained from the leaf (Desta et al., 2020). In a study conducted in Malaysia, the antioxidant status of methanol extract of *P. oleracea* was analyzed in DPPH, FRAP and β-Carotene bleaching tests. As a result of the study, it was reported that the best value was 0.93-5.10 mg GAE/g in the FRAP test (Lim and Quah, 2007). In a study conducted in Spain, it was reported that the ABTS and DPPH percentage results of the methanol extract of *P. oleracea* were 50% and 40%, respectively (Fernández-Poyatos et al., 2021). In another study conducted in Malaysia, the effects of different extracts obtained from *P. oleracea* on DPPH and FRAP were investigated. As a result of the study, LC50 values were reported to be 1.30-1.71 mg/mL and 1.8-4.3 mg GAE/g, respectively (Uddin et al., 2012). In the study conducted in Tunisia, the antioxidant properties of the ethanol extract of *P. oleracea* were investigated using ABTS, diminishing strength test and phosphomolybdenum test. As a result of the evaluation, it was reported by different tests that it is an important source of antioxidants (Dabbou et al., 2020). In

a study conducted in Iran, the alcoholic extract of *P. oleracea* was investigated with DPPH and FRAP tests. As a result of the study, the values were reported to be 13.7-34.3% and 205.3-2749.6 µmol Fe g^{-1} DW, respectively (Saffaryazdi et al., 2020). In another study conducted in Iran, it was reported that the DPPH value of the water-methanolic extract of *P. oleracea* was 15.41-79.06% as a percentage (Jalali Mousavi et al., 2015). In a study conducted in Portugal, it was reported that the FRAP value of *P. oleracea* was 90.6-157.5 mg TE/100 g DW and the LC50 value of the DPPH test was 1-8 mg/mL (Silva and Carvalho, 2014). In a study conducted in Italy, the effect of methanol, hydroalcoholic and ethanol extract of *P. oleracea* on ABTS, DPPH and FRAP was investigated. As a result of the study, it was reported that the best result was LC50 value of 52.86 and 66.98 µg/mL on ABTS and DPPH test in hydroalcoholic extract, respectively (Sicari et al., 2018). In a study conducted in Egypt, the effects of methyl alcohol, ethyl alcohol and water extracts of *P. oleracea* on DPPH, FRAP and β-carotene bleaching tests were investigated. As a result of the study, the values were reported to be 20.20-39.00%, 1.05-3.93% and 43.00-68.21%, respectively (Sallam and Anwar, 2017). In another study conducted in Egypt, the effect of ethanol extract of Portulaca oleracea on DPPH and ABTS was investigated. As a result of the study, LC50 values were reported to be 116.25 and 89.73 µg/mL, respectively (Taha and Osman, 2015). In a study conducted in South Korea, the antioxidant effects of water and ethanol extracts of *P. oleracea* on DPPH, ABTS and FRAP tests were investigated. As a result of the research, it was reported that the best result was 75.53% on ABTS of water extract (Kim et al., 2018). In this context, according to literature data, *P. oleracea* is thought to be an important antioxidant source.

Antimicrobial activity

In recent years, there has been an increase in the number of resistant microorganisms due to unconscious use of antibiotics (Baba et al., 2020). The effectiveness of antimicrobial drugs used in the fight against microorganisms is gradually decreasing (Mohammed et al., 2023b). In this context, the discovery of new antimicrobial drugs has become inevitable. Plants are very important sources of antimicrobials (Bal et al., 2017; Islek et al., 2021). In this study, antimicrobial activity studies of *P. oleracea* reported in the literature were compiled. In a study conducted in South Korea, the antimicrobial activity of water and ethanol extract of *P. oleracea* was investigated. As a result of the study, it was reported that the minimum inhibitory concentration (MIC) values of *Helicobater pylori, Staphylococcus epidermidis, Staphylococcus aureus, Eschericia coli* and *Streptococcus mutans* were 200, 50, 100, 100 and 150 µg/mL, respectively (Cho et al., 2008). In a study conducted in India, the effects of chloroform and ethanol extract of *P. oleracea* on *Staphylococcus aureus, Eschericia*

coli, Pseudomonas aeruginosa, Bacillus cereus, Klebisiella pneumoniae, Aspergillus niger, Aspergillus fumigates and *Nerospora crassa* were investigated by agar diffusion method. As a result of the study, it was reported that the highest zone against *Aspergillus fumigates* in chloroform extract was 18 mm, and in ethanol extract the highest zone was 28 mm (Londonkar and Nayaka, 2011). In a study conducted in South Korea, the antimicrobial status of petroleum ether, chloroform, ethyl acetate and methanol extract of *P. oleracea* was investigated. As a result of the study, ethyl acetate extracts of *P. oleracea* at a concentration of 4,000 ppm showed the highest antimicrobial activity against *Staphylococcus aureus* and *Shigella dysenteriae* (Bae, 2004). In a study conducted in India, the effects of methanol, ethanol, acetone, aqueous and hexane extracts of *P. oleracea* on *Staphylococcus aureus, Eschericia coli, Micrococcus luteus, Aspergillus flavus* and *Fusarium oxysporum* were investigated by disk diffusion method. As a result of the study, it was reported that the best MIC value was 0.14, 0.05, 0.07, 0.62, and 0.73 mg/mL in ethanol extract, respectively (Khursheed and Jain, 2021). A study conducted in Egypt reported that the aqueous extract of *P. oleracea* was effective against pathogenic bacteria and *Candida* species with various MIC values in the range of 12.5−50 µg/mL (Fouda et al., 2022). In a study conducted in Iran, it was reported that the hydroalcoholic extract of *P. oleracea* was effective against *Staphylococcus aureus, Streptococcus pyogenes, Streptococcus pneumoniae, Hafnia alvei, Staphylococcus saprophyticus, Acinetobacter baumannii, Enterococcus faecalis, Proteus mirabilis* and *Serratia marcescens* (Mousavi et al., 2015). In a study conducted in India, the effects of methanol, acetone, ethanol, petroleum ether and n-hexane extract of *P. oleracea* on *Staphylococcus aureus, Escherichia coli, Salmonella typhi, Pseudomonas aeruginosa, Klebsiella pneumoniae, Proteus mirabilis, Salmonella* spp., *Enterococcus faecalis, Citrobacter freundii, Acinetobacter baumannii, Streptococcus pneumoniae, Enterococcus faecium* and *Enterobacter cloacae* were investigated. As a result of the study, it was seen that the highest inhibition zone of methanolic leaf extract was against *Escherichia coli* 26 mm, followed by *Staphylococcus aureus* 24 mm, *Streptococcus pneumoniae* 24 mm, *Klebsiella pneumoniae* 22 mm, *Salmonella typhi* 22 mm. In addition, the maximum inhibition zone in the ethanolic extract was determined to be 22 mm for *Streptococcus pneumoniae*, 20 mm for *Escherichia coli*, 18 mm for *Staphylococcus aureus,* 18 mm for *Citrobacter freundii* and 18 mm for *Klebsiella pneumoniae*. In addition, the lowest MIC value found in the methanolic extract was reported as 0.79 mg/mL against *Staphylococcus aureus, Escherichia coli* and *Streptococcus pneumoniae*. Additionally, the lowest MIC value in ethanolic extract was reported to be 1.56 mg/mL against *Staphylococcus aureus, Escherichia coli, Salmonella typhi*, *Enterococcus faecalis, Acinetobacter baumannii* and *Streptococcus*

pneumoniae (Wasnik and Tumane, 2014). In this context, according to literature data, it has been observed that *P. oleracea* has antimicrobial potential against different microorganisms.

Other activities

It has been reported in the literature that *P. oleracea* has different biological activities in addition to its antioxidant and antimicrobial activities. In this context, in a study conducted in China, (3R)-3,5-bis(3-methoxy-4-hydroxyphenyl)-2,3-dihydro-2(1H)-pyridinone (1) obtained from different extracts of *P. oleracea* and 1,5-dimethyl-6-phenyl-1,2-dihydro-1,2,4-triazin-3(2H)-one alkaloids on K562, MDA-MB-435, MCF-7 and A549 cell lines. LC50 values were reported to be 41.52-222.77 μmol, 120.75->400 μmol, 328.78->400 μmol and 21.76-37.20 μmol, respectively (Tian et al., 2014). In another study conducted in China, it was reported that the LC50 value of homoisoflavonoids obtained from *P. oleracea* on the SGC-7901 cell line was 1.6 μg/mL (Yan et al., 2012). In another study in China, it was reported that POP1, a water-soluble polysaccharide obtained from *P. oleracea*, significantly inhibited the growth of HepG2 cells and Hela cells in vitro (Chen et al., 2010). In a study conducted in Iran, it was reported that *P. oleracea* reduced P53 expression and CDK gene expression in the PANC-1 cancer cell line (Alipour et al., 2022). In a study conducted in Egypt, it was reported that the extract obtained from *P. oleracea* significantly reduced the cell viability of HepG2 and Uo-31 cells in a concentration-dependent manner in its effect on HepG2, Uo-31 and Wi cell lines (Fouda et al., 2022). In a study conducted in India, oral administration of aqueous extract of *P. oleracea* in combination with lycopene was reported to significantly improve CCl4 hepatotoxicity in rats (Anusha et al., 2011). In a study conducted in China, it was reported that the ethanol extract of *P. oleracea* showed anti-aging and anti-inflammatory effects on TNF-α-stimulated NIH3T3/NFκB-Luc cells and an increase in collagen synthesis on NIH3T3 (wild type) cells (Zhang et al., 2009). In another study conducted in China, the EC50 value of *P. oleracea* was reported to be 18.0-497.7 μM through the inhibition of NO production in AW 264.7 cells by isoquinoline alkaloids (Jin et al., 2018). In a study conducted in Iran, the antileishmanial effect of the alcoholic extract of *P. oleracea* was reported to be 360 and 680 μg/mL in terms of LC50 (Eskandari et al., 2016). In a study conducted in China, it was reported that 10E, 12E)-9-ureidooctadeca-10, 12-dienoic acid from Portulaca oleracea named oleraurea has anticholinesterase activity (Xiu et al., 2019). In a study conducted in China, it was determined that *P. oleracea* inhibited UVB-induced apoptotic body formation and apoptosis by downregulating caspase-3 and Bax and upregulating Bcl-2 in VPOP3, mitochondria-mediated signaling pathways. It has also been reported to significantly reduce the expression of microphthalmia-as-

sociated transcription factor, tyrosinase (TYR), and TYR-related protein-1 and TYR-related protein-2 in the melanogenic signaling pathway (Tao et al., 2023). In a study conducted in the Philippines, it was reported that *P. oleracea* extract reduced smooth muscle spasms in the mouse ileum with its antispasmodic effect (Catap et al., 2018). In a study conducted in Iran, it was reported that Portulaca oleracea showed a dose-dependent decrease in the severity of ulcers due to its antiulcerogenic properties (Karimi et al., 2004). In a study conducted in China, it was reported that *P. oleracea* water extract showed anti-IAV activity (Li et al., 2019). In a study conducted in Egypt, it was reported that the petroleum ether extract of *P. oleracea* had an antihyperlipidemic effect on STZ-induced diabetic rats, which could be attributed to its phytosterols, fatty acid and amide compounds (Nazeam et al., 2018). In a study conducted in China, it was reported that the petroleum ether extract of Portulaca oleracea had antihelminthic effects against *Pheretima posthuma* at low doses of 50, 75 and 100 mg/mL (Rao et al., 2013). In a study conducted in Saudi Arabia, it was reported that *P. oleracea* has a herbicidal effect (Al-Humaid and El-Mergawi, 2014). A study conducted in China reported that *P. oleracea* polysaccharide (POL-P3b) has the ability to inhibit cervical cancer cell growth in vitro and in vivo (Zhao et al., 2017). According to this literature data, Portulaca oleracea has been shown to have important biological activities.

Conclusion

In this study, the biological activities, usage areas, mineral and nutritional contents of *P. oleracea* reported in the literature were compiled. According to the literature data obtained, it has been observed that *P. oleracea* has important biological activities such as antioxidant, anticancer and antimicrobial activities. It has also been seen that it can be an important source of health and nutrition. As a result, it is thought that *P. oleracea* may be an important natural source in pharmacological designs.

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CHAPTER 6

BIOLOGICAL ACTIVITIES AND USES OF GENUS *JUNIPERUS*

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Introduction

Humans have primarily benefited from plants for nutrition or treatment purposes according to ancient archaeological findings (Kendir & Güvenç 2010; Mohammed et al., 2022). In the 5000s BC, there were 250 plants identified to be used for therapeutic purposes. Different methods of treatment have been used by the Assyrians, Hittites, Egyptians, Mesopotamians, and Sumerians for many years with plants considered as the most valuable gift given to humans in mythology (Gezgin, 2006; Sevindik et al., 2017; Mohammed et al., 2020a; Korkmaz et al., 2021). Plants used in different fields such as food, cosmetics, pharmacy, phytotherapy, and spices began to be researched and used more frequently after the 1980s as a result of the increase in people's knowledge of health and efforts to protect themselves from the effects of chemical products (Göktaş & Gıdık, 2019; Mohammed et al., 2020b). According to the World Health Organization (WHO), the majority of the world's population initially uses herbal drugs in their search to find solutions to their health problems. However, herbal active ingredients are used in approximately 25% of prescription drugs in developed countries (Farnsworth et al., 1985; Faydaoğlu & Sürücüoğlu, 2011; Mohammed et al., 2018; Mohammed et al., 2019; Mohammed et al., 2021b). The basic products are primary and secondary metabolites, the natural products of plants (Göktaş & Gıdık, 2019; Unal et al., 2022; Uysal et al., 2023), whose parts such as roots, stems, flowers, bulbs, leaves, barks, rhizomes, tubers, and stems are used (Faydaoğlu & Sürücüoğlu, 2011).

Juniperus L. (Tunalier et al., 2002), which grows spontaneously and has 68-80 species and is mostly predominant in the northern hemisphere, extends from Japan and East Asia, from Central Asia and Europe to North America in the west and to the mountains of the African tropics (Adams & Mekee, 1993; Adams & Pandey, 2003; Adams, 2004; Thomas et al., 2007). Members of the genus belonging to the family Cupressaceae are thin-barked, evergreen shrubs, and trees. Its young leaves are pointed and tough, while mature leaves are needle-like. Male flowers have numerous stamens. Female flowers are surrounded by small permanent bracts consisting of 3-8 scales that constitute a hard structure at the base. Seeds are without wings. Fleshy fruits mature between 1-3 years (Davis et al., 1988). It is a species with high ecological tolerance and resistance to the most difficult climatic conditions such as drought and frost (Ünver et al., 2018).

Areas of Use

Members of the genus *Juniperus* have had a wide variety of uses from food to cosmetics since ancient times. Its branches, leaves, and fruits are used for therapeutic purposes among the public, and its essential oils are used in pharmacy for formulating medicines. It is included in lotions and

creams for skin diseases such as psoriasis and eczema, and, with its disinfectant effect, used as a compress for infections. It is used to support metabolism, digestion, stomach, and intestinal diseases and as an anthelmintic, antifungal, diuretic, stimulant, and antiseptic (Acartürk, 1996; Leung and Foster, 1996; Tümen et al., 2012).

Biological activities

Different extracts of different species of the genus *Juniperus* have been used for centuries to treat a variety of medical problems (Schepetkin et al., 2005). This study compiles the biological activities of the species belonging to the genus *Juniperus* reported in the literature. *In vitro* and *in vivo* biological activity studies conducted on species belonging to the genus *Juniperus* have indicated the use of extractions such as acetone, chloroform, methanol, water, steam, acetic acid, and ethyl acetate. Biological activity studies of some species of the genus *Juniperus* are illustrated in Table 1.

Table 1. Biological activity of genus Juniperus

Plant species	**Biological activities**	**Extraction**	**Geographic regions**	**References**
Juniperus scopulorum **Sarg.**	Immunomodulatory activity	Methanol	Montana, ABD	(Schepetkin et al., 2005)
Juniperus phoenicea L.	Antioxidants, antibacterial	Acetone, chloroform, or in mixtures: acetone/water/acetic acid and ethyl acetate/ methanol/water	Thala in mid-west Tunisia	(Hayouni et al., 2007)
Juniperus saltuaria Rehd & Wils, *J. squamata* var. *fargesii* Rehder & E.H.Wilson	Antifungal, insecticidal activity	Gas chromatography—mass spectrometry (GC-MS)	Tibet, China	Wedge et al., 2009)
Juniperus drupacea L.	Antioxidant, antimicrobial	Hexane ve ethyl ether	Syrian	(El-Ghorab et al., 2008)
Juniperus excelsa M.B subsp. *polycarpos* (K. Koch)	Antimicrobial, antifungal, antioxidant	Hydrodistillation	Iran	
Juniperus drupacea Labill.	Antioxidant, cytotoxic potential	Methanol	Türkiye	(Miceli et al., 2011)

Juniperus communis L. var. *communis, Juniperus communis* L. var. *saxatilis Pall., Juniperus drupacea* Labill*, Juniperus oxycedrus* L. subsp. *oxycedrus, Juniperus oxycedrus* L. subsp. *macrocarpa* (Sibth. & Sm.) Ball.	Antimicrobial, anti-biofilm	Methanol extracts, water extracts	Türkiye	(Taviano et al., 2011)
Juniperus excelsa M.Bieb.	Antileishmanial, antitumoral	Methanol	Pakistan	(Nabi et al., 2012)
Juniperus macropoda Boiss. (syn. of *Juniperus polycarpos* K. Koch var. *seravschanica* (Kom.) Kitam.	Antimicrobial, larvicidal	GC-MS, GC-FID	Dalhousie area in Chamba (western Himalaya)	(Stappen et al., 2015)
Juniperus phoenicea L.	Antioxidant	Hexane, methanol	Tunisia	(Keskes et al., 2017)
Juniperus communis L.*,* *J. scopulorum* Sarg.*, J. horizontalis* Moench	Antimicrobial, antioxidant, cytotoxic	Steam distillation	California, ABD	(Elshafie et al., 2020)
Juniperus excelsa subsp. *excelsa* M.Bieb., *Juniperus foetidissima* Willd.	Antimicrobial	Öğütülmüş kuru yapraklar, su distilasyonu yöntemi	Kahramanmaraş, Türkiye	(Taşar et al., 2022)
Juniperus procera Hochst. ex Endl.	Antibacterial and antifungal	Water extract	Al-Baha, Saudi Arabia	(Khan et al., 2022)
Juniperus oxycedrus L. subsp. *oxycedrus, Juniperus communis* L. var. *saxatilis*	Antidiabetic, antimicrobial, antioxidant	Methanol	Erzurun, Türkiye	(Yuca et al., 2023)

Antioxidant activity

Antioxidants are important compounds that reduce the effects of free radicals (Krupodorova and Sevindik, 2020). Oxidative stress occurs as a result of the imbalance between free radicals and the antioxidant defense system (Eraslan et al., 2021). As a result of oxidative stress, many diseases can occur in humans, including cancer, cardiological disorders and neuro-

degenerative diseases (Selamoglu et al., 2020; Akgül et al., 2022). Supplementary antioxidants can be used to reduce the effects of oxidative stress (Pehlivan et al., 2018; Mohammed et al., 2023a; Sevindik et al., 2023) The fruits, seeds, tar, sometimes shoots, and secondary metabolites of the members of the genus *Juniperus* are medically used for their therapeutic properties and inspiration for the development of new drugs. Essential oils and diterpenes present in the members of the genus are the main secondary metabolites, followed by flavonoids, phenolic acids, lignans, coumarins, fatty acids, sterols, tannins, sesquiterpenes, and triterpenes. In addition to the traditional use of the species of this genus, studies on their antioxidant, anticancer, and antidiabetic activities are being carried out as well. Studies prove that the extracts are moderately to significantly active (Aslan Erdem and Ekşi Bona, 2023).

Emami et al. (2008) revealed that the fruit oil of *Juniperus oblonga* M. Bieb had a strong antioxidant effect and the essential oils of the leaves of *J. communis.* subsp. *hemisphaerica* (J.Presl & C.Presl) Nyman had DPPH scavenging activity. Lesjak et al. (2011) investigated the antioxidant properties of the methanol extracts of *Juniperus sibirica* **Burgsdorf›s cones and needles. All tests detected a strong antioxidant effect of the extracts compared to BHT, a well-known synthetic antioxidant.** Menaceur et al. (2013) investigated the essential oils from the leaves and fruits of Algerian *Juniperus phoenicea* L. by the hydrodistillation method and the essential oils from the fruits by Solvent-Free Microwave Assisted Extraction using both capillary GC and GC-MS techniques. They found a relatively weak antioxidant capacity of all essential oils and no improvement in antioxidant activity with the Solvent-Free Microwave Assisted Extraction technique. El Jemli et al. (2016) explained that aqueous extracts of *Juniperus thurifera* L., *Juniperus oxycedrus* L.*, Juniperus phoenicea* L., and *Tetraclinis articulata* (Vahl) Mast. could constitute a new source of natural compounds with antioxidant ability.

Mansour et al. (2023) found the significant anticancer activity of the essential oils from the fruits and leaves of *Juniperus phoenicea* L. against breast and colon cancer cells. Hu et al. (2023) found in their study that the essential oils of *Juniperus formosana* Hayata*, Juniperus przewalskii* Komarov*, Juniperus convallium* Rehder **&** E.H.Wilson*, Juniperus tibetica* Komarov*, Juniperus komarovii* Florin and *Juniperus sabina* from the Qinghai-Tibet Plateau exhibited certain antioxidant effects, and that the species *J. sabina* had the most well-known components (64) and the highest chemo-diversity. Akbulut and Akbulut (2023) evaluated the macro- and micromineral distributions and antioxidant activity of phenolic compounds, organic acid, sugar, methanol, and water extracts of *Juniperus drupace* fruit in their study. The total phenolic content in methanol extracts was

found to be higher than in water extracts and DPPH scavenging activity was found to be higher in methanol extracts.

Antimicrobial activity

Microbial resistance has been increasing in recent years. Accordingly, the effect of antimicrobial drugs used today is insufficient (Baba et al., 2020). Due to the possible side effects of synthetic drugs, people turn to natural drugs (Mohammed et al., 2023b). In this context, researchers have turned to the discovery of new antimicrobial drugs (Akgül et al., 2020; Mohammed et al., 2023c). Natural products are important sources of antimicrobial drugs (Bal et al., 2017; Islek et al., 2021). The identification of very powerful antibacterial and antifungal oils through antimicrobial research is important for more comprehensive activity studies and *in vivo* studies in the future. Pepeljnjak et al., (2005) investigated the antimicrobial effect of the essential oil of the species *Juniperus communis* L. through testing on sixteen bacterial species, seven yeast-like fungi, three yeast, and four dermatophyte strains. The strongest fungicidal activity was recorded against *Candida* spp and dermatophytes. Derwich et al. (2010) investigated the chemical composition and antimicrobial activity of essential oils from *Juniperus phoenica* L. The bacterial strains were observed to be sensitive to the essential oils in the study and indicate a very effective bactericidal activity with minimum inhibitory concentrations ranging from 0.02 to 0.40 mg per mL. Lesjak et al. (2014) found that the phenolic and terpene profiles of the extracts and essential oils of *Juniperus macrocarpa* Sibth. et Sm. (Syn. *Juniperus oxycedrus* L. subsp. *macrocarpa*) exhibited antimicrobial effects against Gram-positive bacteria, especially against the species *Clostridium perfringens*, and suggested their use in food production. Ateş et al. (2015) suggested the aim of developing new natural wood preservatives by studying the antifungal activity of *Juniperus foetidissima* Willd. methanol extract against *Pleurotus ostreatus*. Belov et al. (2023) investigated the biological and chemical activity of extracts of 1- and 2-year-old mature *Juniperus communis* L. fruits obtained by using different solvents such as pentane, chloroform, acetone, methanol, and 70% ethanol under various extraction conditions such as maceration and ultrasound-assisted maceration. They found that the antimicrobial activity was higher in fruits with 1 year of maturity and that the acetone extract obtained through ult-

rasound-assisted maceration had the highest bioactivity compared to phytopathogens.

Other activity

It is reported in the literature that extracts and secondary metabolites from the species Juniperus exhibit different bioactivities. For example, *J. communis* is one of the most frequently studied species in terms of its phytochemical, pharmacological, and therapeutic effects (Al-Snafi, 2018). Samoylenko et al. (2008), in their study with *Juniperus procera* Hochst. ex Endl. fruits, detected that the species exhibited nematicidal and antifouling activities against *Caenorhabditis elegans* and *Artemia salina*. Moujir et al. (2008) investigated the effects of hexane, dichloromethane, acetone, and ethanol extracts of the leaves, bark, and wood of the species *Juniperus brevifolia* on cervix and larynx tumor lines. They determined that the acetone extracts of the leaves, which were soluble in dichloromethane and chloroform, were effective on both tumor cell lines. Fenandez and Cock (2016) investigated the ability of *Juniperus communis* L. extracts prepared using solvents of different polarities to inhibit the growth of a panel of pathogenic bacteria associated with autoimmune inflammatory diseases by disk diffusion test. Methanol, water, and ethyl acetate *J. communis* extracts exhibited moderate to potent growth inhibitory activity against bacterial inducers of rheumatoid arthritis, ankylosing spondylitis, and multiple sclerosis. Methanol and water extracts exhibited the broadest specificity by inhibiting the growth of all bacteria tested. Han and Parker (2017) investigated the anti-inflammatory activity of the essential oil of the species *Juniperus communis* in human dermal fibroblasts. As a result of their study, they found strong anti-inflammatory, immune-modulatory, and wound-healing activities of the essential oil of the species *J. communis* and the effect of this oil on critical genes and pathways associated with metabolism, inflammation, and cancer biology. The authors found in their study that the essential oil of *Juniperus communis* exhibited strong antiproliferative activity and that the oil significantly inhibited tissue remodeling biomarkers, i.e., collagen I, collagen III, and plasminogen activator inhibitor 1 (PAI-I). Lee et al. (2018) stated in their study that *Juniperus rigida* Siebold & Zucc. fruit ethanol extract had anti-atopic properties *in vivo* oxazolone and 2,4-dinitrochlorobenzene (DNCB), caused atopic dermatitis in mouse models, and accelerated the skin barrier healing function. Costa et al. (2018) mentioned the antitrypanosomal properties of *J. oxycedrus* essential oil. Zhang and Yao (2018) explained in their study with male mice that the essential oil of the species *Juniperus virginiana* L. exhibited an anxiolytic effect, but could not prevent anxiety-related behavior in the light-dark box. Semerdjieva et al. (2021) found that the essential oils of the species

Juniperus communis L., *J. oxycedrus* L., *J. pygmaea* C. Koch., and *J. sibirica* Burgsd had significant repellent and insecticidal activity against the species of *Rhopalosiphum padi* (bird cherry-oat aphid) and *Sitobion avenae* (English grain aphid).

Conclusion

In this study, the biological activities of members of the genus Juniperus reported in the literature were compiled. Since different Juniperus species have different pharmacological effects, their biological activities have been studied in a wide range. In addition to its antioxidant and antimicrobial activities, its antitumoral, anti-inflammatory, antiproliferative and anti-atopic activities have also been reported in the literature. It is thought that Juniperus species, which are widely used in public health, can be used in different designs as a pharmacologically important natural material.

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CHAPTER 7

BIOLOGICAL ACTIVITIES OF *MELALEUCA ALTERNIFOLIA*, ALSO KNOWN AS TEA TREE

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Introduction

Plants are unique natural products that are very useful for humanity (Mohammed et al., 2022). Plants were used by humans to make equipment, in wars, as shelter, for heating, nutrition, and in the fight against diseases (Sevindik et al., 2017). Their nutritional properties have put plants at the top of diet lists. In addition to these features, people have used plants to combat different diseases (Mohammed et al., 2020a; Korkmaz et al., 2021). Plants are widely used in methods of combating diseases called traditional and complementary medicine (Mohammed et al., 2020b). Many studies have reported that plants have biological activities such as anticancer, antimicrobial, antioxidant, antiproliferative, anti-inflammatory, hepatoprotective, and DNA protective (Mohammed et al., 2018; Mohammed et al., 2019; Mohammed et al., 2021b; Comlekcioglu et al., 2022; Unal et al., 2022; Kalkan et al., 2023; Uysal et al., 2023). In this context, revealing the biological activity potentials of plants is very important in combating diseases (Pehlivan et al., 2018; Mohammed et al., 2023a). In our study, the biological activities, general properties, areas of use and chemical content of *Melaleuca alternifolia* (Maiden & Betche) Cheel reported in the literature were compiled.

Botany, Geographic distribution and Usage areas

M. alternifolia (Myrtaceae) is known as "tea tree". It is an endemic species generally belonging to Australia. It also grows along streams and in marshy plains on the north coast of south-east Queensland and adjacent parts of New South Wales. Morphologically, tea tree grows up to approximately 7 meters. The leaves are arranged alternately in shape, sometimes scattered or curled. In addition, the leaves are smooth, soft, linear in shape, 10-35 mm long and approximately 1 mm wide. Its flowers are generally found between spring and early summer. The flowers are in clusters of white or cream colored spikes. The flower of M. alternifolia gives the tree a fluffy appearance. It has small, woody, cup-shaped fruits with a diameter of 2-3 mm along the branches. *M. alternifolia* is a very valuable plant, especially due to the richness of oil it contains (Crawford et al., 2004; Carson et al., 2006; Brophy et al., 2013; Sharifi-Rad et al., 2017; de Assis et al., 2020; Kasujja, 2021). Tea tree has been reported to be used to treat coughs, colds, sore throats, acne, as an ointment on open wounds, skin conditions, vaginal infections and dental disorders. It has also been reported that tea tree oil has side effects such as toxicity and coma when swallowed, and may cause skin irritation when used topically in high concentrations (Pena, 1962; Bassett et al., 1990; Shemesh and Mayo, 1991; Carson et al., 2006; Hammer et al., 2006; Oliveira et al., 2011).

Biological activities

Plants contain many biologically active compounds. These features are an indicator of the biological activities of plants (Sevindik et al., 2023). In our study, in vitro and in vivo biological activity studies of *M. alternifolia* reported in the literature were compiled. According to the findings, it was seen that extracts such as essential oil, methanol and hexanal/hexanoic acid were used. It has been observed that the most preferred among these solvents is the essential oil of tea tree. The biological activity study of *M. alternifolia* reported in the literature is shown in table 1.

Table 1. Biological activities of Melaleuca alternifolia

Biological activities	Extraction	Geographic regions	References
Antioxidant, antimicrobial, acaricidal, anti-inflammatory, Insecticidal, antiviral, anthelmintic, antiparasitic, anticancer	Essential oil, methanol, hexanal/ hexanoic acid	China, Serbia, France, Tunisia, Egypt, South Korea, England, Brazil, India, Australia	(Bishop, 1995; Kim et al., 2004; Caldefie-Chézet et al., 2006; Noumi et al., 2011; Thomsen et al., 2011; Nikolić et al., 2012; Grando et al., 2016; Liao et al., 2016; Byahatti et al., 2018; Zhang et al., 2018; Kokina et al., 2019; Puvača et al., 2019; dos Reis et al., 2021; Badr et al., 2023; Sathiyaseelan et al., 2023)

Antioxidant activity

Free radicals are oxidant compounds routinely produced as a result of metabolic activities (Krupodorova and Sevindik, 2020). As levels of these compounds increase, serious cellular damage can occur. The antioxidant defense system plays a role in reducing or suppressing the effects of oxidant compounds (Bal et al., 2019; Gürgen and Sevindik, 2022). Oxidative stress occurs when the balance between oxidant and antioxidant is disrupted. As a result of oxidative stress, serious diseases such as cancer, cardiological disorders, and neurodegenerative diseases can occur in humans (Selamoglu et al., 2020; Saridogan et al., 2021; Bal et al., 2023). Supplementary antioxidants may function in reducing or suppressing the effects of oxidative stress (Eraslan et al., 2021). In this context, it is very important to determine the potential of plants as supplementary antioxidants (Akgül et al., 2022). In our study, the antioxidant activities of *M. alternifolia* reported in the literature were compiled. In this context, in a study conducted in China, the antioxidant status of methanol extract and hexanal/hexanoic

acid extract of *M. alternifolia* was investigated using the DPPH test. As a result of the study, it was reported that the DPPH value of methanol extract was 80% and the DPPH value of hexanal/hexanoic acid extract was 60% (Kim et al., 2004). In another study conducted in China, the antioxidant properties of the essential oil extract of *M. alternifolia* were investigated using DPPH, thiobarbituric acid reactive substances (TBARS) and hydroxyl radical scavenging activity tests. As a result of the study, the values of the tests used were reported to be DPPH EC50 value of 48.35 µg/mL, TBARS LC50 value of 135.9 µg/mL and hydroxyl radical scavenging activity EC50 value of 43.71 µg/mL, respectively (Zhang et al., 2018). In a study conducted in Serbia, it was reported that the free radical scavenging activity of *M. alternifolia* essential oil at 100 and 200 µl/mL concentrations was 60% and 80%, respectively, depending on the concentrations (Puvača et al., 2019). In another study conducted in Serbia, it was reported that the DPPH value range of the essential oil of *M. alternifolia* was 27.74-79.82% (Nikolić et al., 2012). In a study conducted in Tunisia, the antioxidant status of the essential oil of *M. alternifolia* was examined against DPPH, superoxide radicals and β-carotene bleaching tests. Among the tests used in the research, it was reported that the LC50 value of the DPPH test result was 12.5 µg/mL, the LC50 value of the superoxide radicals test result was 26.6 µg/mL, and the LC50 value of the β-carotene bleaching test result was 42 µg/mL (Noumi et al., 2011). In a study conducted in Egypt, it was reported that the EC50 value of the DPPH test result of the essential oil of *M. alternifolia* was 253.65 mg/L (Badr et al., 2023). In a study conducted in South Korea, it was reported that the value ranges of DPPH and ABTS tests of *M. alternifolia*'s essential oil were 80-100% (Sathiyaseelan et al., 2023). In another study conducted in Serbia, the antioxidant status of the essential oil of M. alternifolia was evaluated using DPPH and ABTS tests. As a result of the study, it was reported that the DPPH value was 168.7 mmol/L and the ABTS value was 5.8 mmol/L (Kokina et al., 2019). When literature data were evaluated, it was seen that *M. alternifolia* has antioxidant potential with different methods.

Antimicrobial activity

In recent years, there has been an increase in the number of resistant microorganisms due to unconscious use of antibiotics (Baba et al., 2020). As a result, antimicrobial drugs used against microorganisms are insufficient (Mohammed et al., 2023b). Nowadays, interest in the discovery of new antimicrobial drugs for use in combating microbial diseases is increasing (Bal et al., 2017; Islek et al., 2021). In this context, it is very important to determine the potential of plants as natural sources of new antimicrobial drugs. In this study, antimicrobial activity studies of *M. alternifolia* reported in the literature were compiled. In a study conducted in

China, it was reported that the antimicrobial potential of *M. alternifolia* essential oil against *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Penicillium italicum* and *Penicillium digitatum* strains ranged between 8-24 mg/mL (Zhang et al., 2018). In a study conducted in Serbia, the MIC values of the essential oil of *M. alternifolia* against *Escherichia coli, Staphylococcus aureus, Aspergillus fumigatus* and *Candida albicans* were reported to be between 0.05-1.78 mg/mL (Puvača et al., 2019). In another study conducted in Serbia, the antimicrobial status of the essential oil of *M. alternifolia* against *Escherichia coli, Pseudomonas aeruginosa, Salmonella typhimurium, Enterococcus cloacae, Bacillus cereus, Micrococcus flavus, Listeria monocytogenes, Staphylococcus aureus, Aspergillus ochraceus, Aspergillus fumigatus, Aspergillus niger, Aspergillus flavus, Penicillium funiculosum, Penicillium ochrochloron, Fusarium verticiloides, Trichoderma viride* and *Candida albicans* strains was investigated. As a result of the study, it was reported that the MIC and MBC-MFC value ranges were 0.5-18 mg/mL and 1-36.5 mg/mL, respectively (Nikolić et al., 2012). In a study conducted in Tunisia, it was reported that the essential oil of *M. alternifolia* was effective against *Candida albicans, Candida parapsilosis, Candida kefyr, Candida glabrata, Candida dubliniensis* and *Candida lusitaniae* strains (Noumi et al., 2011). In a study conducted in Egypt, the MIC value of the essential oil of *M. alternifolia* against *Salmonella typhimurium* and *Staphylococcus aureus* bacteria was reported to be 600 and 475 mg/L, respectively. Additionally, the EC50 value against *Candida albicans, Aspergillus flavus* and *Aspergillus niger* strains was reported to be 74.86 mg/L, 253.13 mg/L and 312.53 mg/L, respectively (Badr et al., 2023). In a study conducted in South Korea, it was reported that the MIC values of the essential oil of *M. alternifolia* against *Bacillus cereus, Staphylococcus aureus, Escherichia col*i and *Salmonella enterica* strains ranged between 31.25-250 µg/mL (Sathiyaseelan et al., 2023). In another study conducted in Serbia, it was reported that the MIC and MBC values of *M. alternifolia* essential oil were 10 and >10 µg/mL for *Staphylococcus aureus* and 10 and 10 µg/mL for *Salmonella Typhimurium* (Kokina et al., 2019). In a study conducted in Australia, it was reported that the inhibition zone range of *M. alternifolia* essential oil against *Escherichia coli, Staphylococcus aureus, Salmonella typhimurium, Pseudomonas aeruginosa* and *Candida albicans* strains was 0-49.8 mm (Thomsen et al., 2011). When literature data were evaluated, it was seen that *M. alternifolia* has antimicrobial potential against different microorganisms.

Other activities

It has been observed in the literature that *M. alternifolia* has different biological activities in addition to its antioxidant and antimicrobial activities. In this context, in a study conducted in Serbia, the acaricidal status of

the essential oil of *M. alternifolia* was investigated. As a result of the study, it was reported that its effectiveness against Ixodes ricinus and *Dermanyssus gallinae* was 60% and 80%, respectively (Puvača et al., 2019). In a study conducted in France, the anti-inflammatory status of the essential oil of *M. alternifolia* was analyzed. As a result of the study, it was found that it was ineffective on the chemotaxis of isolated neutrophils (PMNs), as revealed by the decrease in IL-2 secretion by stimulated lymphocytes, and inhibited the proliferation of peripheral blood mononuclear cells (PBMC). This 0.1% essential oil is anti-inflammatory. The cytokine has been reported to directly increase IL-4 secretion compared to IL-4 secretion without essential oil (18.5 vs. 3.3, $p < 0.05$) and also increases IL-10 secretion by 0.01% (Caldefie-Chézet et al., 2006). In a study conducted in China, the insecticidal status of the essential oil of *M. alternifolia* against *Sitophilus zeamais*, known as corn weevil, was investigated. As a result of the study, it was reported that its essential oil has fumigant toxicity against *S. zeamais* and terpinen-4-ol as a component is the most effective compound for fumigant toxicity (Liao et al., 2016). In a study conducted in England, the antiviral status of *M. alternifolia* essential oil against tobacco mosaic virus was investigated. As a result of the study, it was reported that when the oil was applied to *Nicotiana glutinosa* plants as a pre-inoculation spray at 100, 250 and 500 ppm, it significantly reduced the number of lesions for at least 10 days after inoculation (Bishop, 1995). In a study conducted in Brazil, it was reported that the essential oil of M. alternifolia had an anthelmintic effect against *Haemonchus contortus* (Grando et al., 2016). In another study conducted in Brazil, it was reported that the essential oil of *M. alternifolia* has an antiparasitic supportive effect on Rhamdia quelen, which was exposed to the insecticide amitraz, thanks to the diets added as a growth promoter (dos Reis et al., 2021). In a study conducted in India, the LC50 value of *M. alternifolia* essential oil as an anticancer on the colon cancer cell line (HT29) was reported to be 12.5 µg/mL (Byahatti et al., 2018). In this context, according to literature data, it has been observed that *M. alternifolia* has important biological activities.

Chemical Contents

Secondary metabolites are compounds produced in natural products that do not have nutritional properties but are medically important. The type and amount of these compounds strengthen the medicinal potential of the natural product (Akgül et al., 2020; Mohammed et al., 2023c). In this study, the chemical contents of *M. alternifolia* reported in the literature were determined. For essential oil content studies on *M. alternifolia*, the aerial, leaves and seed parts of the plant were generally used. The essential oil content of *M. alternifolia* species is shown in table 2.

Table 2. Essential oil contents of Melaleuca alternifolia

Geographic regions	**Used Part**	**Essential oil content**	**Reference**
Slovakia, Egypt, Australia, China, Tunisia, Turkey, Cameroon, Serbia, Italy, Spain, India	Aerial, leaves, seed	terpinen-4-ol (17.31-46.9%), γ-terpinene (10.0-28.0%), 1,8-cineole (1.83-37.0%), p-cymene (0.5-12%), α-terpinene (3.9-13.0%), α-terpineol (2.8-20.24%), α-pinene (1.0-21.64%), α-terpinolene (1.5-27.3%), aromadendrene (0.1-7.0%), ledene (1.9%), δ-cadinene (1.5-1.9%), α-limonene (0.5-9.37%), β-pinene (0.7-23.3%), sabinene (3.5%), globulol (0.5-3.0%), viridiflorol (0.6-1.5%), o-cymene (6.54 %), β-phellandrene (1.9%), β-copaene (1.6%)	(Verghese et al., 1996; Hart et al., 2000; Carson and Riley, 2001; Southwell and Russell, 2002; Noumi et al., 2011; Benelli et al., 2013; Gómez-Rincón et al., 2014; Liao et al., 2017; Nikolić et al., 2017; Labib et al., 2019; Alfred Ngenge et al., 2021; Sevik et al., 2021; Borotová et al., 2022; Ramachandran et al., 2023)

As a result of the literature research, it was seen that the main components in the essential oil content of *M. alternifolia* species were terpinen-4-ol (17.31-46.9%), γ-terpinene (10.0-28.0%), 1,8-cineole (1.83-37.0%), p-cymene (0.5-12%), α-terpinene (3.9-13.0%), α-terpineol (2.8-20.24%)), α-pinene (1.0-21.64%), α-terpinolene (1.5-27.3%), aromadendrene (0.1-7.0%), ledene (1.9%), δ-cadinene (1.5-1.9%), α-limonene (0.5-9.37%), β-pinene (0.7-23.3%), sabinene (3.5%), globulol (0.5-3.0%), viridifluorol (0.6-1.5%), o-cymene (6.54%), β-phellandrene (1.9%) and β-copaene (1.6%) (Verghese et al., 1996; Hart et al., 2000; Carson and Riley, 2001; Southwell and Russell, 2002; Noumi et al., 2011; Benelli et al., 2013; Gómez-Rincón et al., 2014; Liao et al., 2017; Nikolić et al., 2017; Labib et al., 2019; Alfred Ngenge et al., 2021; Sevik et al., 2021; Borotová et al., 2022; Ramachandran et al., 2023). Bu kapsamda bitki bünyesinde bulunan bileşikler açısından dogal kaynak olabileceği düşünülmektedir.

Conclusion

In this study, the biological activities and chemical contents of *M. alternifolia* reported in the literature were compiled. Additionally, the usage areas and general characteristics of the plant are presented. As a result of the literature research, it was seen that the plant has potential for use in pharmacological fields. It has been observed that it can be an important natural source of antioxidant, antimicrobial and anticancer activity. As a result, it has been seen that the plant can be used as a natural material in pharmacological designs.

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CHAPTER 8

ALGAE AS A FUNCTIONAL NATURAL PRODUCT: *SPIRULINA*

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Introduction

Nets, which are among the most common organisms in the world, have the potential to reproduce even under very extreme conditions. They can be distributed in terrestrial ecosystems, aquatic ecosystems, fresh water, salt water and many different ecosystems. It is estimated that the number of known algae species worldwide is close to 1 million. There are approximately 150 thousand officially described species (Guiry 2012). Morphologically, single-celled organisms can vary in size from 3 to 10 μm. Additionally, in macro terms, they can be up to 70 m long (El Gamal 2010). Many studies have shown that algae have biological activities such as anticancer, antimicrobial, antiproliferative, antidiabetic and antioxidant (Noda et al., 1990; Schaeffer and Krylov, 2000; Kelman et al., 2012; Torrest et al., 2014; Kausalya and Rao, 2015; Zheng et al., 2023). In this context, in this study, the biological activities of Spirulina reported in the literature were compiled.

Spirulina

Spirulina is the name given to the dried mass of Arthrospira species. It is a very rich food source obtained from Arthrospira platensis and A. maxima species and grown in many parts of the world. It is generally sold in the market in the form of capsules, tablets or powder and as a dietary supplement. It has low fat and calorie content. It is also a source of essential amino acids. It can serve to prevent the weakening effects caused by diabetes, anemia and air pollution. It can be used in the prevention of cardiological diseases, anti-aging, and health problems such as cancer, arthritis and cataracts. Spirulina contains A (Beta-carotene), B1 (thiamine), B2 (riboflavin), B3 (niacin), B6 (pyridoxine), B12 (cobalamin), C, D, E, folate, K, biotin, pantothenic acid, There are vitamins such as inositol. It also contains elements such as calcium, manganese, iron, chromium, phosphorus, molybdenum, iodine, chloride, magnesium, sodium, zinc, potassium, selenium, germanium, copper and boron (Cohen, 1997; Vonshak, 1997; Khan et al., 2005; Ali and Saleh, 2012; Soni et al., 2017).

Biological activities

Dogan products produce many biologically active compounds. These bioactive compounds are medically important secondary metabolites (Sevindik et al., 2023). In this study, the biological activities of Spirulina reported in the literature were compiled. The findings obtained are shown in table 1.

Table 1. Biological activities of Spirulina

Biological activities	Extraction	Geographic regions	References
Antioxidant, antimicrobial, anticancer, antiviral, anti-inflammatory, cytotoxic	Phycocyanobilin, methanol, protean, water, polysaccharide, ethanol, diethyl ether, ethyl acetate, petroleum ether, petroleum ether, chloroform, acetone	Japan, Brazil, Egypt, Spain, Thailand, Taiwan, India, Algeria, USA, Iran	(Miranda et al., 1998 ; Hirata et al., 2000; Estrada et al., 2001; Wu et al., 2005; Abd El-Baky et al., 2008; Chaiklahan et al., 2013; El-Baz et al., 2013; El-Sheekh et al., 2014; Usharani et al., 2015; Al-Ghanayem, 2017; Shalaby and Shanab, 2013; Pham et al., 2016; Akbarizare et al., 2020; Kumar et al., 2022; Bachir et al., 2023)

Antioxidant activity

As a result of metabolic processes, living organisms routinely produce oxidant compounds (Krupodorova and Sevindik, 2020). When levels of oxidant compounds are low, they can be tolerated by living things. However, as its levels increase, it can be quite harmful (Bal et al., 2019; Gürgen and Sevindik, 2022). As the levels of oxidant compounds increase, antioxidants come into play and suppress it. Oxidative stress occurs as a result of the imbalance between oxidant compounds and antioxidants. As a result of oxidative stress, serious diseases such as cancer and neurological disorders may occur (Selamoglu et al., 2020; Saridogan et al., 2021; Bal et al., 2023). Supplementary antioxidants can serve to reduce the effects of oxidative stress (Eraslan et al., 2021; Akgül et al., 2022). In this context, the potential of Spirulina as an antioxidant supplement was evaluated. In a study conducted in Japan, the antioxidative activity of phycocyanobilin obtained from Spirulina Platensis was analyzed against the oxidation of methyl linoleate in a hydrophobic system or with phosphatidylcholine liposomes. As a result of the study, it was determined that when the concentrations of phycocyanobilin and phycocyanobilin in the reaction mixture were adjusted equally on the basis of phycocyanobilin to scavenge radicals from AAPH and prevent the initiation of radical chain reactions, the activity of phycocyanobilin was almost the same as that of phycocyanin in the reaction mixture containing AAPH. Additionally, the antioxidant effect of phycocyanin prepared from spray-dried Spirulina was almost the same as that of phycocyanin prepared from fresh Spirulina. As a result, it has been reported that phycocyanobilin is responsible for the majority of the

antioxidant activity of phycocyanin and can serve as an effective antioxidant in a living human body (Hirata et al., 2000). In a study conducted in Brazil, the antioxidant activity of methanol extract obtained from Spirulina maxima, a microalgae rich in protein and other essential nutrients, was investigated in vitro and in vivo. As a result of the study, it was reported that the LC50 (the concentration that causes a 50% reduction in oxidation) of the extract was 0.18 mg/mL. In addition, for in vivo antioxidant capacity, plasma antioxidant capacity in the plasma and liver of animals receiving a daily dose of 5 mg for 2 and 7 weeks was measured in brain homogenate incubated at 37oC for 1 hour. After 2 hours of incubation at 37oC in the control and experimental groups, the production of oxidized compounds in the liver was measured in terms of thiobarbituric acid reactant substances (TBARS), and the antioxidant capacity of the plasma after treatment was found to be 71% for the experimental group and 54% for the control group. As a result, it was reported that the data obtained from liver spontaneous peroxidation studies did not show any significant difference between the groups (Miranda et al., 1998). In a study conducted in Egypt, the increased content of some bioactive compounds of Spirulina Platensis grown in medium containing various hydrogen peroxide concentrations (2, 4, 6 and 8 mM) as a model for environmental stress was analyzed. As a result of the study, it was determined that there was a positive correlation between the increase in H2O2 and the increasing amounts of cellular lipophilic antioxidants (total carotenoids and α-tocopherol) and hydrophilic antioxidants [glutathione (GSH) and ascorbic acid (AsA)]. It has also been reported that *S. platensis* behaves with different strategies against dose-dependent H2O2 exposure and its responses are strongly associated with scavenging enzymes (SOD, CAT, PX and APX) and antioxidant compounds (GSH, AsA, β-carotene, astaxanthin and astaxanthin) (Abd El-Baky et al., 2008). In a study conducted in Spain, the antioxidant status of the protean extract obtained from the planktonic blue-green algae *Spirulina platensis* was evaluated. As a result of the research, in evaluating the antioxidant activity of different fractions obtained during the phycocyanin purification process through the scavenging activity of the hydroxyl radical, it was reported that the increase in phycocyanin content was associated with the increase in antioxidant activity in different fractions and therefore the phycobiliprotein phycocyanin was the component mainly responsible for the antioxidant activity (Estrada et al., 2001). In another study conducted in Egypt, the antioxidant properties of water, absolute methanol and 50% methanol in water extract obtained from Spirulina Platensis were investigated in the DPPH and ABTS test. As a result of the study, it was reported that the DPPH value was 14.22-95.3% as a percentage and the ABTS value was 77.60-99.55% as a percentage (Shalaby and Shanab, 2013). In a study conducted in Thailand, it was reported that the polysaccharide extract obtained from

the sample used exhibited antioxidant properties (Chaiklahan et al., 2013). In a study conducted in Taiwan, it was reported that the antioxidant activity of spirulina determined by the ABTS method of the extract obtained from the sample was EC50= 72.44 µmol trolox equivalent/g and the antioxidant activity of spirulina determined by the DPPH method was EC50= 19.39 µmol ascorbic acid equivalent/g (Wu et al., 2005). In a study conducted in India, it was reported that significant enzymatic antioxidant activity was observed for the ethanol extract obtained from the sample used, but aqueous extracts were higher in terms of catalase, SOD and GPx activity, and the same trend was observed for non-enzymatic activities (Kumar et al., 2022).

Antimicrobial activity

Nowadays, there is an increase in the number of resistant microorganisms due to unconscious use of antibiotics (Baba et al., 2020). In this context, the discovery of new antimicrobial drugs is inevitable (Mohammed et al., 2023b). Due to the possible side effects of synthetic drugs, researchers have turned to natural antimicrobial sources (Bal et al., 2017; Islek et al., 2021). In this context, the antimicrobial activities of *Spirulina* reported in the literature have been compiled. Minimal inhibitory concentration of diethyl ether, ethyl acetate, petroleum ether, petroleum ether and chloroform extract obtained from the sample used in a study conducted in Egypt on *Bacillus subtilis, Staphyllococcus aureus, Pseudomonas aeruginosa, Eschrichia coli*, *Candida albicans, Aspergillus flavous* and *Aspergillus niger* strains (MICs) and Minimal cidal concentration (MCCs) value were analyzed. As a result of the study, it was determined that the Gram-positive bacterium *Bacillus subtilis* was the most sensitive bacterial species, while the Gram-negative bacterium P. *aeruginosa* was the least sensitive bacterial species, while the purified antibiotic produced by *S.platensis* was more effective against Gram-positive, Gram-negative bacteria and single-celled fungi. Additionally, *C. albicans* was determined to be the most sensitive test strains with a minimum inhibition concentration of 30.0µg ml-1. In addition, the Gram-negative bacterium *P. aeruginosa* was the least sensitive (MIC, 85µg ml-1), while the most resistant isolates were reported to be the multicellular fungi *A. flavus* and *A. niger* (El-Sheekh et al., 2014). In a study conducted in India, the antimicrobial status of methanol, acetone, ethanol, hexane and petroleum ether extract obtained from *Spirulina* sample against *Staphylococcus aureus, Streptococcus epidermidis*, *Streptococcus pyogenes, Bacillus cereus, Proteus mirabilis, Escherichia coli, Pseudomonas aeruginosa, Vibrio cholerae, Salmonella typhi, Klebsiella pneumoniae, Shigella flexneri, Aspergillus flavus, Aspergillus niger, Aspergillus fumigatus, Candida tropicalis, Candida albicans* and *Candida glabrata* was investigated. As a result of the study, the inhibition zone value of the samples used was reported to be between 9-20 mm, respectively

(Usharani et al., 2015). In another study conducted in Egypt, disk diffusion method was used to demonstrate the antimicrobial effect of the ethanol extract of *Spirulina platensis* against different bacterial strains, *Escherichia coli, Staphylococcus aureus, Salmonella typhi* and *Enterococcus faecalis*, as well as *Candida albicans*. As a result of the study, it was reported that inhibition occurred only in *Enterococcus faecalis* and *Candida albicans* species (El-Baz et al., 2013). In a study conducted in Saudi Arabia, the antimicrobial status of ethanol, methanol and aqueous extracts of *Spirulina plantensis* against *Staphylococcus aureus, Streptococcus pneumoniae, Bacilluscereus, Enterococcus faecalis, Pseudomonas aureginosa, Proteus vulgaris, Salmonella typhi, Enterobacter cloacae, Klebsiella pneumoniae, Escherichia coli* and *Candida* sp was investigated. As a result of the study, it was reported that all these algae extracts inhibited the growth of all microbes to varying degrees regardless of their type, the methanol extract showed a strong effect and exhibited superior antibacterial activity against all bacterial species, especially Gram-positive bacteria. (Al-Ghanayem, 2017). In a study conducted in Algeria, it was reported that acetone and diethyl ether extracts obtained from the sample showed the strongest antibacterial activity against gram-positive and gram-negative bacteria, and only acetone extract showed antifungal activity against *Fusarium culmorum* (Bachir et al., 2023).

Other activities

Liver fibrosis is a chronic liver disease that will develop into cirrhosis if serious damage continues. A potential treatment for liver fibrosis has been investigated by inhibiting activated hepatic stellate cell (HSC) proliferation and growth inhibitory status on human liver cancer cells HepG2. As a result of the study, it was reported that it showed antiproliferative effects on HSC and HepG2, and Annexin-V staining showed that the aqueous extract of spirulina induced the apoptosis of HSC after 12 hours of treatment, and the aqueous extract of spirulina triggered cell cycle arrest in the G2/M phase (Wu et al. , 2005). In another study conducted in Egypt, it was reported that the ethanol extract of Spirulina platensis had a 53.3%, 66.7%, 76.7%, 56.7% and 50% reduction in vitro against adenovirus type 7, Coxsackievirus B4, astrovirus type 1, rotavirus Wa strain and adenovirus type 40, respectively (El-Baz et al. ., 2013). A study conducted in America investigated whether the regulation of histone deacetylases (HDACs) plays a role in the anti-inflammatory effect of Spirulina Platensis (SPE) in macrophages. As a result of the study, it was reported that treatment of macrophages with SPE rapidly and dose-dependently decreased HDAC2, 3 and 4 proteins, which preceded decreases in mRNA levels, and degradation of HDAC4 protein was attenuated in the presence of calpain protease inhibitors, lysosomal acidification and Ca2+/calmodulin-dependent

protein kinase II, respectively. Furthermore, Acetylated histone H3 was increased in SPE-treated macrophages to a similar level as in macrophages treated with a pan-HDAC inhibitor, and concomitant inhibition of inflammatory gene expression upon LPS stimulation was achieved, while knockdown of HDAC3 resulted in basal and LPS-induced pro-inflammatory gene expression. increased its expression. Knockdown of HDAC4 increased basal expression of interleukin-1β (IL-1β). However, it has been reported to attenuate LPS-induced inflammatory gene expression, Chromatin immunoprecipitation, p65 binding and H3K9/K14 acetylation at the Il-1β and tumor necrosis factor α (Tnfa) promoters of SPE (Pham et al., 2016). In a study conducted in Iran, it was determined that all tested extracts and compounds showed an inhibitory effect on the viability of HepG2 cells in a dose-dependent manner, without cytotoxicity on normal cells. It has also been reported that the strongest anticancer activity was induced by alkaloids (2 mg/ml), with an 80% reduction in cell viability and an LC50 of 0.53 mg/ml, and the LC50 values of the aqueous extract, methanolic extract, and phenolic compounds were 1.7, 1.28, and 0.86 mg/ml, respectively (Akbarizare et al., 2020).

Conclusion

In this study, the biological activities and usage areas of Spirulina reported in the literature were compiled. As a result of literature research, it has been observed that algae has significant antioxidant, antimicrobial and anticancer activities. In this context, Spirulina is thought to be an important natural material in pharmacological designs.

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CHAPTER 9

COPULA IMPLEMENTATION WITH GAMMA REGRESSION USING INSURANCE DATA

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INTRODUCTION

Statistical modeling commences with delineating the data necessary for predictions. Nowadays, researchers are faced with a large data set for modeling and prediction with real case studies. Various analytical techniques provide valuable solutions for researchers across different fields and applications. Combining different analytical techniques together allows us to obtain more information from the data. In this study, it is aimed to obtain statistical models containing more information by using the gamma regression and copula functions together with the latest developments in the literature.

Copula functions were originally mentioned in the literature by Sklar in 1959. Nelson (1999) also explained the mathematical theoretic background of the copula functions in details in his book. Copula functions are frequently used to understand the relationships between multivariate responses. The fundamental idea of the copula functions is the based on expressing joint distribution function using marginal distributions. The absence of a constraint on marginal distributions increases the mathematical flexibility of copula functions.

Copula functions' varied statistical applications are becoming more common in literature. Applications of copula models are employed in the fundamental areas such as finance, insurance, health, demography and natural sciences. Genest and Favre (2007) explained the joint distribution modeling of several random variables coming from hydrological event data. Their work is also one of the main references that contains copula application examples in the literature in a simple and comprehensive way. Parsa and Klugman (2011) used copula functions with regression-based models as an alternative copula model for simulated data. Chen et al. (2015) created multiple mortality models with copula and time series approach for mortality risk pricing.

Actuarial science statistical modeling depended heavily on oversimplified assumptions for a considerable amount of time. The simplicity of the multivariate normal distribution made it the

preferred option. Normal distribution and also linear regression does not provide an adequate approximation to many data sets. Typically, researchers work with long-tailed and skewed data in actuarial applications.

In the realm of insurance markets, defining claim severity accurately is pivotal for managing pricing and reserves. Claim severity refers the amount of loss which is associated with an insurance claim. Insurance companies want to estimate how many claims they may expect to see and how much the cost of the claims they may expect to pay for policyholders. Carriere (2000), Frees and Valdez (2008), Luciano et al. (2008) and Joe (2014) are a few notable examples of the copula functions' applications in data modeling in the actuarial area.

This study analyses the variables that influence claim severity in auto traffic insurance data and discovers the dependency structure between two claim amounts. In the first section of the study, copula functions used in modeling the dependence between random variables are introduced. Then the main copula types are explained. Subsequently, the transition to joint structure methodology steps is summarized. Moving to the application section, the methodology for the marginal models and copula model is implemented on the insurance data after its introduction. In the conclusion part, it is emphasized that why the dependence structure revealed is important.

Definition of The Copula Function:

Copula is a multivariate function with uniform marginals. (u_1, $u_2, \dots, u_p$) are uniform variables on (0,1). p - dimensional copula distribution function is defined as

$$C(u_1, u_2, \dots, u_p) = \Pr(U_1 \leq u_1, \dots, U_p \leq u_p). \qquad (1)$$

Any continuous random variable can be uniform across (0,1) using its probability integral transformation (Yan, 2007).

Sklar Theorem

Sklar theorem shows any multivariate function can be written by a copula function.

(F_1 , F_2, …, F_n) marginal distribution functions, G n dimensional distribution function is defined with following equation.

$$G(x_1, \dots, x_n) = C\big(F_1(x_1), \dots, F_n(x_n)\big) \qquad (2)$$

The equation demonstrates that a copula function can be used to express any cumulative distribution function. (Sklar, 1973, p. 451)

According to Sklar's theorem; there is a single copula function with continuous marginal distributions. This is mostly because the probability integral transform construction lacks a discrete analogue. Some conversions are needed to be able to use Sklar's theorem with discrete random variables. Ruschendorf (2009) and Nikoloulopoulos (2013) carried out qualified studies on the transformation of discrete random variables. It is focused on continuous case in this study.

Copula is generally used to obtain joint distribution from marginal distributions functions. Special conditions for two-variable copula function ($0 \leq u_1 \leq 1$ and $0 \leq u_2 \leq 1$) :

1. $C[0, u_2] = C[u_1, 0] = 0$

2. $C[1, u_2] = C[u_1, 1] = 1$

3. $\boldsymbol{C}$, is an increasing function

(Besis, 2002).

For two dimensional case, a copula distribution and density function with uniform marginals can be written with equation 3 and 4 (Denuit et. al, 2005, p.201).

$$C(u_1, u_2) = \Pr(U_1 \leq u_1, U_2 \leq u_2) \qquad (3)$$

$$c(u_1, u_2) = \frac{\partial^2 C(u)}{\partial u_1 \, \partial u_2}, \; u \in (0,1)^2 \qquad (4)$$

TYPES OF COPULA FUNCTIONS

There are several families of copulas have been described in the literature. Two main families of the copula faimilies are ***Archimedian copulas*** and ***Elliptical copulas*** (Nelson, 1999).

Archimedean family is introduced by Genest and MacKay (1986a) as a sub-family of the copula functions. The Archimedean copula is constructed by a generator function; $\phi(t)$ and different generator functions produce specific Archimedean copulas. Some important special

cases of Archimedean copulas are Frank copula, Clayton/Cook - Johnson copula, Gumbel - Hougaard copula.

Frank Copula:

This copula has a simple analytic structure and can represent both positive and negative dependency. Frank copula (distribution function) is

$$C_\alpha(u_1, u_2) = -\frac{1}{\alpha}\ln\left(1 + \frac{(\exp(-\alpha u_1)-1)(\exp(-\alpha u_2)-1)}{\exp(-\alpha)-1}\right),\ \alpha \neq 0. \quad (5)$$

α ; dependency parameter in the equation. For positive values it shows positive dependency, while for negative values it shows negative dependency. When α is equal to zero, copula will transform into independence copula (Denuit et al., 2005, p.205). Under independency assumption, copula distribution function is

$$C(u_1, u_2) = u_1\, u_2. \quad (6)$$

(Denuit et al., 2005, p.196).

Bivariate Archimedian copula functions with their generator functions are listed in the Table 1 (Frees and Valdez, 1998).

Table 1: Bivariate Archimedian Copula Functions with their generator functions.

Family	Generator $\phi(t)$	Dependence parameter α	Bivariate Copula $C_\phi(u, v)$
Clayton/ Cook-Johnson	$t^{-\alpha} - 1$	$\alpha > 1$	$(u^{-\alpha} + v^{-\alpha} - 1)^{-1/\alpha}$
Gumbel - Hougaard	$(-\ln t)^\alpha$	$\alpha \geq 1$	$\exp\{-[(-\ln u)^\alpha + (-\ln v)^\alpha]^{1/\alpha}\}$
Frank	$\ln\frac{e^{\alpha t} - 1}{e^\alpha - 1}$	$-\infty < \alpha < \infty$	$\frac{1}{\alpha}\ln\left(1 + \frac{(e^{\alpha u} - 1)(e^{\alpha v} - 1)}{e^\alpha - 1}\right)$

Different values of the dependency parameter of an Archimedian copula mean different dependence structure between random varibles. It is observed that when α increases, dependence structure gets close to maximum dependency for Clayton/ Cook-Johnson copula function. The dependence parameter contains all of the information regarding the dependency between marginals.

Elliptical Copulas:

Copulas derived from multivariate elliptic distributions are known as elliptic copulas. Normal (Gaussian) copula ve t- copula are the main copula families of the elliptic copulas. Normal copula is structured with multivariate normal distribution and t-copula, on the other hand, is structured with a multivariate t distribution.

Normal Copula:

Φ and ϕ in the equation; denote the standard normal distribution and density functions. Normal (Gaussian) copula density function is

$$c_N(u_1,\dots,u_p) = \phi_N\left(\Phi^{-1}(u_1),\dots,\Phi^{-1}(u_p)\right)\prod_{j=1}^{p}\frac{1}{\phi\left(\Phi^{-1}(u_j)\right)}. \quad (7)$$

Two-dimensional Normal copula distribution function is

$$C(u_1,u_2) = \Phi_G(\Phi^{-1}(u_1),\Phi^{-1}(u_2);\theta) = \int_{-\infty}^{\Phi^{-1}(u_1)}\int_{-\infty}^{\Phi^{-1}(u_2)}\frac{1}{2\pi\sqrt{1-\theta^2}} * \left(\frac{-\left(s^2-2\theta st+t^2\right)}{2(1-\theta^2)}\right) dsdt. \quad (8)$$

The θ parameter expresses the degree and direction of dependence. Normal copula is a flexible copula function as it allows for positive and negative dependency (Karadağ, 2008).

t Copula:

t-copula is especially prefered when lower and upper tail dependence is observed in the data. In recent years, it is used in the fields of finance applications such as stocks pricing, portfolio valuation. t copula generator density function is

$$g(t) = \frac{\Gamma\left(\frac{v+d}{2}\right)}{(\pi v)^{\frac{d}{2}}\Gamma\left(\frac{v}{2}\right)}\left(1+\frac{t}{v}\right)^{-\frac{v+d}{2}},\ t \in [0,\infty) \qquad (9)$$

(Hofert et al., 2018, p.89).

t-copula is also used on financial time series since it captures tail dependency effectively. Patton (2012)'s work gives a review of copula based time series models with parametric and non-parametric methods.

TRANSITION TO JOINT STRUCTURE

Multivariate distribution function can be defined using the copula and copula structure does not restrict the choice of marginal distributions. After the selection of the univariate model in the first step, candidate copula functions should be determined and evaluated to model the dependency structure. The process of copula modeling for continuous variables can be summarised with two steps:

Firstly, consider arbitrary marginal distribution functions: $F_1(y_1), \dots, F_n(y_n)$.

Secondly, define multivariate distribution function using the copula function (Sklar's Theorem): $G(y_1, \dots, y_n) = C\left(F_1(y_1), \dots, F_n(y_n)\right)$.

APPLICATION

Claim severity data is analyzed regarding the dependence structure between response variables in this study. The data is a cross-sectional sub-set of the four year motor third liability insurance policy data that is provided by one of the Turkish private insurance companies. This data set consists of 2775 insurance policyholders's demographic information, claim amounts and auto technical characteristics for each policy.

Response variables: Injury claim and auto damage claim (Y_1, Y_2).

Explanatory variables: age of policyholder, gender, martial status, days of the policy, age of the car, maxspeed, speedingtime, length, width, height, torque, horsepower, enginevolume, curbweight.

R- 4.3.2 statistical programming is used to make application part of the study. "copula" package is chosen as the fundamental package to model dependency between claim amounts.

Firstly, association between two different response variables (Y_1, Y_2) is checked with calculating Spearman's correlation coefficient.

Spearman's rho: 0.185

Marginal Models:

Gamma distribution is an important distribution to model claim severity data in the actuarial science literature. $\mu_i = \frac{v}{\lambda_i}$, $\sigma^2 = \frac{1}{v}$ are mean and variance of Gamma distribution, respectively. Gamma distribution's log-likelihood function with (μ, σ^2) is

$$l(\mu, v, y) = (v-1)\log(y) - \frac{v}{\mu}y + v\log\, v - v\log\, \mu - \log\, \Gamma(v). \quad (10)$$

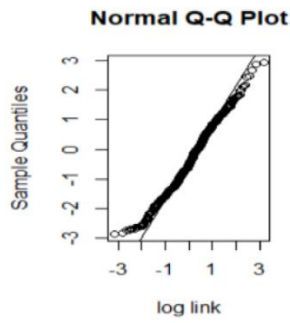
The log-likelihood function of Gamma regression model with log-link function ($\mu_i = \exp\{\boldsymbol{x_i\beta}\}$):

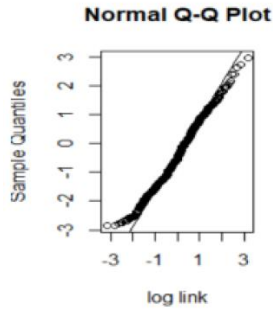
$$l(y; \mu, v) = \sum_{i=1}^{n} \left\{ \frac{y_i/\exp(x_i\beta) + x_i\beta}{-v} + \frac{v+1}{v}\ln\, y_i - \frac{\ln\, v}{v} - \ln\, \Gamma\left(\frac{1}{v}\right) \right\} \quad (11)$$

(Czado, 2012).

Here; Gamma regression model is applied for injury claims and auto damage claims since claim severity showed skewed distributions. Amounts claimed for positive values are taken into account. Maximum likelihood estimation methos is applied to estimate model parameters.

QQ (quantile-quantile) graphs are used to evaluate the compliance of Gamma model with the claim amount data. QQ plot compares the quantile values of the estimated distrubution and sample quantiles.





Gamma regression model is chosen as marginals according to QQ graphs of Y_1 *and* Y_2, which expresses the amount injury claims and auto damage claims.

Injury claim Gamma fitting results:

According to first gamma regression model estimation results; the coefficients of "days of the policy", "age of the car", "car status", "length", "width", "torque" and "enginevolume" is obtained statistically significant (*%95 confidence levels).

```
Coefficients:
              Estimate Std. Error t value Pr(>|t|)
(Intercept)  11.5233959  2.4302850   4.742 2.63e-06 ***
Gender        0.0053628  0.1080731   0.050   0.9604
days         -0.0010945  0.0005253  -2.084   0.0376 *
age          -0.0020239  0.0038884  -0.520   0.6029
martial2     -0.1105877  0.1307993  -0.845   0.3982
martial3     -0.3435523  0.3334697  -1.030   0.3033
martial4      0.2552297  0.3024626   0.844   0.3991
martial5      0.1203400  0.1525118   0.789   0.4304
car_age       0.0216478  0.0119235   1.816   0.0699 .
status2      -0.1824526  0.1082448  -1.686   0.0924 .
maxspeed     -0.0121122  0.0078845  -1.536   0.1250
speedingtime -0.0115859  0.0445104  -0.260   0.7947
length        0.0004483  0.0002530   1.772   0.0769 .
width         0.0003787  0.0005819   0.651   0.5154
height       -0.0012326  0.0008691  -1.418   0.1566
torque        0.0030032  0.0012264   2.449   0.0146 *
horsepower    0.0050784  0.0044389   1.144   0.2530
enginevolume -0.0007845  0.0003096  -2.534   0.0115 *
curbweight   -0.0003579  0.0004852  -0.738   0.4610
```

Auto damage claim Gamma fitting results:

According to second gamma regression model estimation results; the coefficients of "gender", "age of the car", "martial status", "maxspeed" and "curbweight" is obtained statistically significant (*%95 confidence levels).

```
Coefficients:
             Estimate Std. Error t value Pr(>|t|)
(Intercept) 11.3238449  2.3241782   4.872 1.4e-06 ***
Gender      -0.1430929  0.1033546  -1.384   0.1667 *
days        -0.0003290  0.0005023  -0.655   0.5128
age         -0.0065112  0.0037187  -1.751   0.0804 *
martial2     0.0671406  0.1250886   0.537   0.5916 .
martial3    -0.1899423  0.3189103  -0.596   0.5517
martial4     0.3145715  0.2892570   1.088   0.2772
martial5    -0.1531282  0.1458531  -1.050   0.2942
car_age     -0.0098976  0.0114029  -0.868   0.3857
status2      0.0916482  0.1035188   0.885   0.3763
maxspeed     0.0017827  0.0075403   0.236   0.8132 *
speedingtime 0.0500597  0.0425671   1.176   0.2400
length       0.0001754  0.0002420   0.725   0.4689
width        0.0000353  0.0005565   0.063   0.9494
height      -0.0007660  0.0008312  -0.922   0.3571
torque      -0.0001351  0.0011728  -0.115   0.9083
horsepower   0.0027960  0.0042451   0.659   0.5104
enginevolume 0.0001725  0.0002961   0.583   0.5603
curbweight  -0.0002921  0.0004640  -0.629   0.5293 .
```

Copula Model:

Bivariate joint distribution function can be written in terms of copula function:

$$G(y_1, y_2) = C\big(F_1(y_1), F_2(y_2)\big). \qquad (12)$$

Then, bivariate density function can be expressed with the copula function and marginal distribution functions:

$$\mathrm{f}_{y,12} = c\big(F_1(y_1), F_2(y_2)\big) \times \prod_{i=1}^{2} f_i(y_i). \qquad (13)$$

After getting scale and shape parameters from fitted values of Gamma regression, y_1 variable and y_2 variable are transformed to the U[0,1] using the probability integral transformation with the fitted gamma distribution's parameters.

Speearman correlation is checked for uniform transforms (u_1, u_2) in Table 2:

Table 2: Dependency matrix

	u_1	u_2
u_1	1.000	0.187
u_2	0.187	1.00

By transforming to uniforms, the association is maintained. Frank copula is a considerable copula function to use in the joint model here, since positive dependency between the response variables is observed. Frank copula is applied to the transformed response variables using

maximum likelihood estimation method. Dependency parameter results for Frank copula is written in Table 3:

Table 3:Fitted dependency parameters values

Dependency parameter $\boldsymbol{\theta}$	1.225
Rho (fittedfrank.cop)	0.202

Spearman's rho (0.20) is close to previous calculated spearman correlation value (0.18). By using copula function in the joint model, assosiation is kept. The idea is updating the copula parameter with fitted parameters and calculating Spearman's correlation coefficient of the fitted copula.

Normal copula is applied as another copula to check the dependency structure between response variables. Dependency parameter result for Normal copula is

Rho (fittedfrank.cop): 0.187.

Dependency parameter which is coming from Normal copula is more close to the dependency between the response variables. Bivariate distribution function can be chosen Normal copula with Gamma marginals for future predicition studies.

CONCLUDING REMARKS

Ignoring dependency structure between response variables affects the statistical estimated values. In this study, positive dependency is found between injury claim amount and auto damage claim amount variables. Although dependency seems weak, keeping the dependency structure is taken into consideration when specifying the joint distribution model. Features that appear small in financial data can cause significant differences on the estimation part. It is important to get maximum statistical information from the financial data to produce less risky estimations. For example in the insurance industry, ignoring the

dependeny between different risks may cause underestimation / overestimation of insurance premiums.

The dependency structure between two different types of claim amounts is modeled with Frank and Normal copula function. It is aimed to observe that keeping the dependecy structure regardless of the marginal models by copula functions. It is also exampled here that the researcher may also prefer regression method when creating the marginal models. Combining copula model and regression method together will give more information how explanatory variables affect the response variables in a dependency concept.

Gamma regression is applied for marginal models and Normal copula is chosen to keep dependency structure between claim amounts. Copula function compounds marginal models without any constrain on marginal distributions. Researchers can apply alternative marginal models for severity data, and estimate joint claim amount by using the copula model in the further studies.

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CHAPTER 10

CARBON FIBER REINFORCED POLYMERS (CFRPS) AND RECENT TRENDS TOWARDS THEIR USE IN HYBRID STRUCTURES: A REVIEW

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1. Introduction

There has been an ever-increasing trend in the replacement of metal structures with high strength to weight-ratio materials to reduce the overall weight of several components and systems in high-tech industries such as automotive, aviation, defense, etc. In the course of this search, carbon fiber reinforced polymers (CFRPs), also known as carbon fiber reinforced plastics, have found wide application as a result of their superior mechanical properties and competitive characteristics over other materials and composites due to the superior characteristics of carbon-fiber and the various advantages and countless possibilities for enabled by use of polymer materials as the structural matrix. With the advent of additive manufacturing technologies, the potential for CFRPs is further expanded since the manufacturers are liberated from the requirement for use of molding technologies with higher expenses coupled with longer design and realization periods despite the mass production advantage of molding. However, compared to mass production, the ever-increasing need for specialized and customized components for specialized component and service suppliers required to keep the pace with Industry 4.0 environment demanding more flexible and rapid production processes for rapid product-cycles brings forward the importance of additive manufacturing technologies in key high-tech industries, in which case CFRPs hold the utmost importance. CFRPs were first introduced in 1960s to replace the key structural components in aviation industry (Hegde et al., 2019) and since then they gained both academic and commercial interest due to the mentioned tremendous potential they offer. Since then, the global annual production of CFRPs gradually increased with the drop of CFRP production expenses and the advent of 3D printing technologies. Apart from their use for structural airframe applications in aviation industry (Rahim & Sasahara, 2018), their application involves their extended use as structural material in maritime, automotive, construction industries, sports equipment, oil and gas industry, etc. Development of composite materials and structures involving single or blend polymer matrices and organic or inorganic reinforcement materials in the form of fibers, whiskers, particles and nanoparticles, is another popular research area which also overlaps with the realm of CFRPs. Thus, the design of CFRPs is not limited to the combination of a single matrix with a single reinforcement, namely carbon fiber. Hybrid structure of CFRPs may involve organic or inorganic various other reinforcements in fiber or particle form, blends of two or more polymer matrices, combination of CFRPs with other materials, or even the use of various types of protective coatings over CFRP. Thus, the present work aims to give brief fundamental information about carbon-fiber reinforced polymers and their applications regardless of whether they are molded or 3D printed, the types of polymer

matrices and carbon fiber reinforcements used in these composite materials, and finally the recent research trends about CFRPs with hybrid structures, which may involve incorporation of another reinforcement, matrix, material or protective coatings.

2. Carbon Fiber Reinforced Polymers (CFRPs)

Carbon fiber reinforced polymer composites are composed of a carbon fiber reinforcement among a variety of forms (such as continuous CF or short CF) and a polymer matrix or blend polymer matrices as the structural component. Polymer matrix provide toughness and structural integrity whereas the carbon fiber reinforcement enhances the mechanical properties of polymer in correlation with the fiber orientation. The biggest advantage of CFRPs for structural applications in industries such as automotive and aviation is the mass reduction achieved in comparison with metal or alloy components. Moreover, CFRPs' resistance against corrosive environments makes them highly qualified for applications where their metal or alloy counterparts suffer corrosion-related failures. The properties of obtained composites can be tailored by varying the various physical properties and the direction of fiber component and the type of the polymer used. The properties of the materials also rely on the type of the manufacturing process applied.

2.1. Manufacturing Methods for CFRPs

Manufacturing methods for CFRPs can be roughly categorized as automatized and non-automatized methods. Non-automatized methods involve hand layup and spray layup molding processes (Ayanul, 2019) and these processes still find wide application among a variety of industries. These processes can also be automatized by use of robotic or automatic equipment.

Hand Layup Molding:

This process is often referred to as wet-hand layup in the case of CFRP production and involve the application of compression molding or vacuum bagging techniques to manufacture cross-ply laminates from prepreg fabrics (Chen et al., 2021)these composites boast high specific stiffnesses and specific strengths. However, current limitations on manufacturing, which vary greatly based on the technology that is utilized, restrict access to composite materials in a variety of applications. Traditional wet hand-layups offer a large diversity of viable constituent materials, but the fabrication geometry is limited and the manual process is time-consuming. In contrast, fiber 3D-printing (F3DP. Prepreg fabrics are preprocessed mixture of reinforcement (fabric) and uncured resin (*Prepreg Materials - Composite*

Envisions), and cross-ply laminate is the notation for stacking of laminate layers with 0° and 90° fiber orientation (Types of Laminates, comsol.com). In this method, dry fibers are bonded together in woven or knitted form. The bonded form of fibers is thus often referred to as fabrics. The fabrics are then placed by hand in a mold and the uncured resin of the polymer is applied upon the fabric (Jamir et al., 2018). Full impregnation and bonding of resin with the fabric is ensured first by application of a roller and/or by applying vacuum or pressure. A schematic diagram of the process is shown in Figure 1.

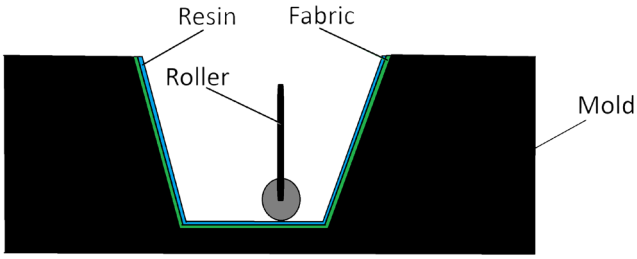

Figure 1. *Schematic representation of hand-layup process (Hand Lay-Up - CORE Molding Technologies)*

Spray Layup Molding:

Spray layup or spray up molding is basically the same method with hand layup except the uncured resin is not placed manually but by the help of a handgun, by which both the resin and the chopped fiber are sprayed upon the mold surface. It is a commonly applied method for finishing large products and components (Balasubramanian et al., 2018). Depending on the structural requirements of the produced component, hand layup and spray layup methods are often applied together and up to 15-25% fiber volume ratios can be achieved by these methods (Knight & Curliss, 2003). Although it requires less labor than hand layup, spray-up technique limits the application of carbon-fibers to chopped fibers or short fibers only, due to its operating principle. Most of the resins are capable of being cured under room temperature and this method allows the production of large components or materials (S. J. Park & Seo, 2011).

Compression Molding:

Compression molding was initially used for molding thermoset polymers and rubber in the early 20th century and since then it has been one of the most common methods for manufacturing polymers and polymer composites (C. H. Park & Lee, 2012). In compression molding, sheet molding compounds (SMC) as rectangular pre-prepared byproducts with high strength are shaped by conventional compression molding technique.

Mold has two halves, the bottom half is fixed and the upper half moves with the upper platen (Ayanul, 2019). This method has advantages such as high production rates, low labor costs, low scrap material etc. over the other composite polymer manufacturing techniques. Its disadvantages are the requirement for more equipment, its inability to mold transparent polymers, and low product lives for sheet molding compounds (C. H. Park & Lee, 2012).

Injection Molding:

Injection molding techniques used in the manufacturing of composite polymers can be categorized as screw type injection molding operating by the rotation of a screw or screws to convey the matrix- fiber mixture, plunger type injection molding in which a plunger enables the transfer of matrix-fiber mixture to the mold, and reaction injection molding where reactants are fed in a pressurized chamber to form the polymer product (Ayanul, 2019). Injection molding method, particularly the screw type injection molding, has been one of the most common and efficient methods to form polymer composites or polymer blends via melt compounding under shear forces enabled by altered consecutive screw forms.

2.2. Common Polymers Used as Matrix in CFRPs

Almost all thermosets and thermoplastics are applied as the binding matrix for manufacturing CFRPs. The type of the matrix material depends on the structural and functional requirements for the finished product. Among thermoset polymers, epoxy (polyepoxide) is the most common material used in CFRPs whereas thermoplastics such as nylon, polyester and vinyl ester are common thermoplastics reinforced with carbon fiber (Kudo et al., 2023)herein, we investigate the relationship between fatigue and an epoxy resin used in CFRPs. Generally, fatigue is related to the entropy, which comprises the mechanical entropy, calculated from the dissipated energy and temperature, and thermal entropy, calculated from the relationship between specific heat capacity and temperature. According to previous studies, mechanical entropy generation and thermal entropy generation are equal. Herein, 100 cyclic loading tests are conducted on epoxy resin specimens consisting of 4,4’-DDS and bisphenol a diglycidyl ether. The dissipated energy is determined based on stress–strain curves, and mechanical entropy generation is quantified. An equation for the relationship between the specific heat capacity and temperature is developed based on the Debye model, and the increase in specific heat capacity is calculated for equal mechanical and thermal entropy generations. Generally, differential scanning calorimetry is used for specific heat capacity measurements; however, because these measurements are performed by cutting the specimen, a nondestructive measurement method is required. In this study, the

specific heat capacity is measured using lock-in thermography (LIT.

2.3. Production and Common Types of Carbon Fiber Reinforcement in CFRPs

Carbon fibers can be obtained from precursors in fiber form having a carbon backbone and with the ability to yield a carbon residue upon pyrolysis (Donnet et al., 2003) resulting in fibers with at least 90% carbon content (Pusch & Wohlmann, 2018)high stiffness, low density, and a high chemical resistance. All these advantages can be combined with an adequate (polymer resin. The types of carbon fibers are dependent of upon the precursors used for production. Those derived from organic precursors such as polyacrylonitrile (PAN), is the most common one (Bajpai, 2021), anisotropic mesophase pitch and isotropic pitch are produced through spinning of the precursors, whereas those derived from vapor-grown precursors are produced via decomposing the vapor of organic precursors by thermal decomposition (Inagaki, 2000). Carbon fibers are available in a wide variety of physical forms, including continuous and short fibers, woven fabrics and non-woven fabrics, tapes, woven preforms, hybrid clothes and braids (Manocha, 2001). Carbon fibers are also categorized in terms of the mechanical properties they provide, as ultrahigh modulus (UHM), ultrahigh strength (UHS), high modulus (HM) and high strength (HS) carbon fibers (Bajpai, 2021).

3. An Overview of Recent Literature Works on CFRPs with Hybrid Structures

As also mentioned in the introduction section of the present review study, CFRPs have found application in a wide variety of industries as the application of carbon fiber reinforcements is not limited to the reinforcement of polymer matrices. However, the present work is limited with the studies on use of CRFPs in combination with non-polymer materials, or those with multiple matrix and reinforcement constituents.

Huang et al. (2021) performed a comparative study on the dynamic and quasi-static bending characteristics and collapse behavior of aluminum-CFRP hybrid beams under different loading conditions. They concluded after the numerical and experimental investigations that, the specific energy absorption could be enhanced by nearly 70% by varying the wrapping angles and loading conditions. The mean

crashing force error between the experimental and numerical results were reported to be less than 7%, and reported that the main factor affecting the energy absorbing behavior of Al/CFRP beams were the loading condition and the CFRP layout (Huang et al., 2021).

Another work on Al-CFRP hybrid structures was conducted by Bellini et al. (2021), who investigated the failure modes related with flexural loads. They performed three point bending tests on specimens with and without adhesive interfaces between the aluminum sheets and CFRP layers. After the performed experiments they reported that, the fracture mode and the surface morphology resulting from the fracture mode were primarily affected by the presence of the applied adhesive (Bellini et al., 2021).

Hasa and Pinho (2019) introduced an innovative Al-CFRP hybrid composite in which a bio-inspired lamellar structure was used to preserve the structural integrity. The proposed novel hybrid crossed-lamellar structure was reported to achieve large curvatures without compromising its structural integrity while enabling energy dissipation in stable conditions (Häsä & Pinho, 2019).

Pan et al. (2021) proposed a novel method for analysis of damage mechanism of integrally braided CFRP and hybrid composite tubes made of CFRP/Al which were exposed to transverse impact. They used a thermography technique to evaluate the transverse impact load condition which enabled monitoring of progressive thermomechanical behavior. Their numerical and experimental studies revealed that, the hybrid structure was advantageous in many aspects such as providing the structure with diverse mechanical properties and enabling a coordinated specific energy absorption mechanism (Pan et al., 2021).

In a recent research related to construction sector, Han et al. (2023) performed compression tests on concrete columns strengthened with chlorinated polyvinyl chloride (PVC) -CFRP hybrid tubes and engineered cementitious composite (ECC) layers to explore

the compressive behavior of the designed system. Reportedly, the concrete cylinder samples strengthened with the proposed hybrid system were found to have superior load carrying capacity as well as ductility (Han et al., 2023).

Ye et al. (2020) performed experimental and numerical investigations on the crushing behaviors of KFRP/CFRP hybrid laminate pre-folded tubes which were subjected to quasi-static axial loads. Reportedly, the composite tube's energy absorption behavior was strongly correlated with the composition of the hybrid filler (Ye et al., 2020).

In another work related to hybrid concrete structures, Sohail et al. (2022) investigated the effectiveness of the impressed current technique on lab-scale reinforced concrete (RC) samples to assess the response of beams subject to severe corrosion and strengthened with hybrid CFRP and glass FRP (GFRP) structures. Reportedly, their work was distinguished by application of the technique on corroded and strengthened RC beams. Reportedly, after application of impressed current on RC samples for a period of 15 days, respectively 32% and 30% reduction in the yield strength and ultimate strength of RC beams were observed, which were higher than those of the control beams. Also, compared to the degraded beams, respectively 36% and 42% average gain in yield and ultimate loads was achieved with single CFRP laminate, whereas 42% and 62% higher yield load and ultimate load were exhibited by the beams strengthened with CFRP-GFRP hybrid laminates, showing that CFRP and CFRP-GFRP laminates were effective for strengthening and rehabilitation for RCs subject to severe corrosion (Ghous Sohail et al., 2022).

Zhu et al. (2020) performed a comparative study on hybrid metal/CFRP structures subject to static and dynamic loading and investigated the crushing behavior of Al/CFRP tubes with different hybrid designs. They examined the energy-absorbing mechanisms as well as the factors effective on the hybrid tubes' crashworthiness. Reportedly, the main energy absorbing mechanism was the outer

aluminum tube's external inversion mode, in which case the increasing thickness of CFRP layers reduced the outer aluminum tube's contribution to total energy absorption (Zhu et al., 2020).

Fallah et al. (2020) deposited hybrid metallic coatings on CFRPs via hybrid cold spray deposition-copper electroplating process and deposited copper to enhance the electrical properties of CFRPs. Reportedly, deposition of copper was possible provided that a copper interlayer is formed, which also provides the CFRP from being damaged and enables the cold spraying of copper particles with ease when compared to conventional cold spraying (Fallah et al., 2020).

Li et al. (2022) investigated the low-velocity impact response of CFRP-elastomer-metal hybrid laminates against that of conventional fiber-metal laminates with numerical and experimental studies. They concluded that, after they introduced elastomer into the structure, larger portion of the laminate contributed to the overall load bearing performance. Moreover, introduction of elastomer also affected each component's energy absorption performance (Li et al., 2022).

Melaibari et al. (2022) proposed a sandwich composite laminate with a CFRP/dyneema core to improve the impact resistance and tolerance of the composites. For this purpose they designed a hybrid intraply core to draw on the superior elasticity and stiffness/weight ratio of dyneema fibers. The conducted mechanical tests showed that, the damages that were initiated as delamination and local matrix cracks at the impacted face of CFRP was distributed in the through-thickness direction of the laminates of monolith CFRP samples. Also, in monolith CFRP composite, the fiber cut was initiated at lower plies as a result of high bending normal strains, whereas, in the case of sandwich composites, the high compressive stresses were initiated in the upper CFRP plies as fiber kinking. They concluded that, the sandwich composite exhibited higher CAI strength compared to the monolithic CFRP structures as a result of lower damage level in sandwich laminates (Melaibari et al., 2022).

Lu et al. (2021) performed a research study on evaluation of the energy absorption behavior of hybrid CFRP/aluminum square tubes under axial loading condition. They studied the crushing behavior and advantages of variable thickness hybrid square (VTHS) tubes in which CFRP laminates with varying thickness were used to improve axial crushing behavior. They reported that, when compared with hybrid square tubes having uniform thickness, VTHS exhibited lower initial peak crushing force, and VTHS provided 24.5% improvement in specific energy absorption. They also verified the accuracy of the experimental tests by employing a theoretical model (Lu et al., 2021).

Muflikhun et al. (2020) evaluated the mechanical performance and failure mode response of carbon fiber reinforced plastic – steel plate cold commercial (CFRP-SPCC) thin hybrid laminates via flexural and tensile tests by applying four different types of adhesives. They used differential scanning calorimetry (DSC) and Fourier-transform infrared spectroscopy (FTIR) for characterization. As a result of the performed tests, they reported that, addition of SPCC laminates into the composite delayed the CFRP laminates' premature failure by up to 58.5%. Addition of SPCC layers also shifted the failure mode to adhesive breakage from premature fiber breakage (Muflikhun et al., 2020).

4. Conclusion

The brief overview of the literature works on hybrid CFRP structures reveal that, the studies involve in-depth performance and failure evaluation of hybrid CFRP structures for reinforcing civil engineering structures, the structures used in aviation and transportation industries, as well as those related to enhance several properties of CFRPs such as improving electrical performance by application of thermal spray coatings to deposit metal powders. The variety of subjects and disciplines involved in the application of CFRP composites reveal that, although carbon fiber reinforced polymers have been around for quite a time now, the limits of the possibilities that these magnificent composites offer are yet to be explored.

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