

A Comprehensive Review of the Medicinal and Pharmacological Importance and Future Perspectives of *Monothea buxifolia*

Laila Noor*, Ghulam Dastagir†, Muhammad Naseer‡, Sumaira Noor§

Abstract

Monothea buxifolia (*M. buxifolia*) a valued plant in traditional medicine, has attracted considerable scientific interest for its remarkable therapeutic potential. This review presents a comprehensive account of the plant's pharmacological activities and phytochemical profile. Extensive studies reveal that *M. buxifolia* exhibits a broad spectrum of pharmacological properties, including antioxidant, antinociceptive, antimicrobial, antifungal, antileishmanial, antipyretic, anti-inflammatory, hepatoprotective, antimalarial, anti-arthritic, and renal-protective effects. Its strong antioxidant activity is largely attributed to a rich array of phytochemicals such as flavonoids, alkaloids, saponins, terpenoids, and anthraquinones, which effectively scavenge free radicals and mitigate oxidative stress, thereby safeguarding against numerous diseases. Flavonoids and alkaloids contribute significantly to the plant's antinociceptive and analgesic effects, highlighting its promise in pain management. Moreover, *M. buxifolia* exhibits potent antimicrobial and antifungal activities, underscoring its potential as a natural remedy for infectious diseases. Its hepatoprotective benefits, primarily due to saponins and flavonoids, further enhance its therapeutic value, as do its anti-inflammatory and antipyretic actions. Notably, the plant shows promising antimalarial and anti-arthritic effects and offers protective benefits against renal toxicity. Given its diverse and potent phytochemical composition, *M. buxifolia* stands out as a compelling candidate for the development of novel natural therapeutics targeting a wide range of health conditions.

Keywords: *Monothea buxifolia*, Phytochemicals, Pharmacological Activities, Traditional medicine.

Introduction

Infectious diseases remain a major global challenge, causing nearly 57 million deaths each year (Akhtar et al., 2018). Medicinal plants have been used for healing since ancient times and are the basis of many home remedies. The term “medicinal plants” refers to diverse plant species used in traditional medicine, many with proven therapeutic properties (Raut et al., 2014). Today, over 70,000 plant species are used medicinally,

*Pharmacognosy Laboratory, Department of Botany, University of Peshawar, Peshawar 25120, Pakistan, li1904152@gmail.com

†Pharmacognosy Laboratory Department of Botany, University of Peshawar, Peshawar 25120, Pakistan, dastagirbotany@yahoo.com

‡Corresponding Author: Department of Chemical and Life Sciences, Qurtuba University of Science & IT, Peshawar 25100, Pakistan, naseerkhan6912@gmail.com

§Pharmacognosy Laboratory, Department of Botany, University of Peshawar, Peshawar 25120, Pakistan, suamiranoor04@gmail.com

attracting attention as effective and affordable natural treatment options (Patel et al., 2023).

According to the World Health Organization, over 30% of the world's plant species have medicinal uses (Rai et al., 2022). Approximately 11% of the 252 essential medicines are plant-derived, and the WHO recognizes herbal therapy as a core component of primary healthcare (Shakya et al., 2016; Adil et al., 2024). More than 20,000 plant species—with sustainable cultivation across diverse climates—possess therapeutic properties (Thakur et al., 2020). These species produce a rich array of secondary metabolites (phytochemicals) such as alkaloids, flavonoids, saponins, terpenoids, steroids, glycosides, tannins, and volatile oils, many of which have proven efficacy against numerous ailments. Notable medicinal families include Caryophyllaceae, Lamiaceae, Asteraceae, Cucurbitaceae, Lythraceae, and Sapotaceae.

These properties are linked to bioactive compounds in certain plant families (Chandra et al., 2015; Uritu et al., 2018; Isgor et al., 2015; Rajasree et al., 2016; Florence et al., 2015; Khayi et al., 2020). Sapotaceae is abundant in tropical regions, especially South American rainforests, and is among the most diverse families in lowland forests (Terra-Araujo et al., 2015). *M. buxifolia*, a broad-leaved evergreen tree, grows in hilly areas of Afghanistan, Yemen, Oman, Iran, Saudi Arabia, and northwest Pakistan, where it's known locally as Gurguray (Ali et al., 2023). In Pakistan, Sapotaceae includes six genera and seven species, with *M. buxifolia* as the only native species (Nazir et al., 2020).

M. buxifolia is a versatile plant that grows either as a spiny evergreen tree or a large thorny shrub, with two forms distinguished by fruit color. It can reach up to 10 meters in height, with white pubescent flowers and dark-green leaves, flowering from April to May and fruiting from June to August (Rashid et al., 2019). Traditionally, it has been widely used to treat infectious diseases (Ali et al., 2022). Its fruit, commonly sold in local markets, has laxative, digestive, and anti-helminthic properties (Burki et al., 2019).

The leaves contain secondary metabolites with pharmacological effects, including laxative, vermifuge, purgative, hematinic, antipyretic, and anticancer activities, as well as reducing sugars (Ali et al., 2020). The plant is used for digestive issues, bacterial infections, wounds, and urinary disorders due to its digestive, laxative, antipyretic, hepatoprotective, analgesic, anti-inflammatory, and antioxidant properties (Hassan et al., 2019; Ali et al., 2022) (Figure 1, Table 1).

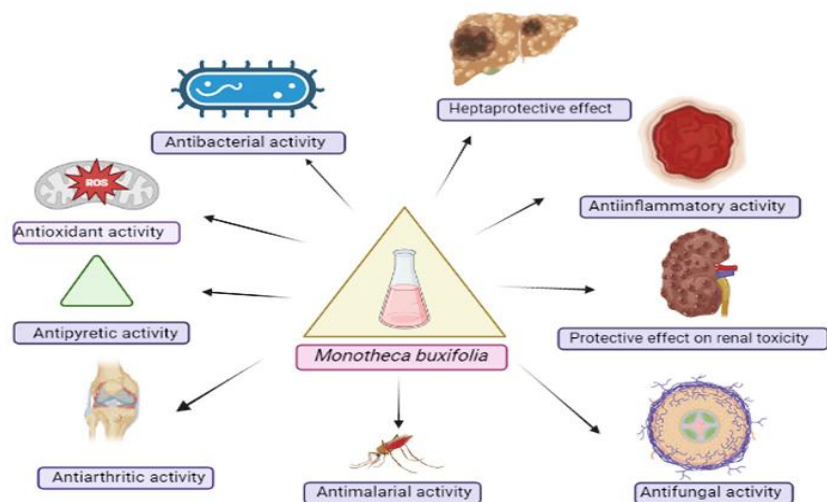


Figure 1: Effects of *Monotheca buxifolia* on various activities revealing its potential medicinal properties.

Table 1: Pharmacological activities of *Monotheca buxifolia*.

S. No.	Activities	Part used	Extract	Conclusion	References
01	Antioxidant	Fruit	Methanol, n-butanol and aqueous fraction	The n-butanol, aqueous and methanol fractions possessed high amount of phenolic and flavonoids compared with other fractions, and subsequently showed a pronounced scavenging activity	Jan et al. (2013)
02	Antinociceptive	Fruit	Hydro-ethanolic extract	MBHE's antinociceptive properties as a final observation Oleanolic acid and isoquercetin concentration in <i>M. buxifolia</i> result in increased antinociceptive action.	Ullah et al. (2016)
03	Antimicrobial	Leaves	Fruit extract	Gram-positive and gram-negative bacteria's cell walls are scraped by <i>M. buxifolia</i> leaf extract's antibacterial action, whereas gram positive bacteria close suffered significant damage to the biofilm.	Burki et al. (2019)
04	Antipyretic	Fruit	Hydro ethanolic extract	It has been suggested that <i>M. buxifolia</i> significant antipyretic efficacy is at least partially attributable to the presence of isoquercetin and oleanolic acid in the plant.	Jan et al. (2013)
05	Anti-inflammatory	Bark, stem	Hydro-ethanolic extract	This plant has historically successfully been applied therapeutically by local people to relieve inflammation	Ullah et al. (2016)

06	Hepatoprotective effect	Fruit	Hydro ethanolic extract	Rats exposed to the drugs isoniazid and rifampicin developed liver damage, and <i>M. buxifolia</i> fruit is found to have hepatoprotective properties.	Ullah et al. (2016)
07	Antimalarial	Plant	Methanolic extract	The maximum inhibition results of methanolic fraction of <i>M. buxifolia</i> against Plasmodium	Din et al. (2018)
08	Anti-arthritis	Plant	Methanolic extract	The anti-arthritis activity of the plant has been pharmacologically assessed by <i>M. buxifolia</i> extract.	Akhtar et al. (2021)
09	Protective effect of <i>M. buxifolia</i> on Renal toxicity.	Leaves	Methanolic extract	Plant extract with dietary polyphenols has the capacity to protect rats from renal damage caused by CCl ₄ .	Khan et al.,2012

Antioxidant Activity

Oxidative stress occurs when there is an imbalance between the production of reactive oxygen species (ROS) and the body's ability to neutralize them with antioxidants (Helliwell et al., 2007). ROS are byproducts of cellular processes like respiration, metabolism, and immune activity (Cyran et al., 2022). Free radicals, which are unstable molecules with unpaired electrons, react readily with proteins, lipids, DNA, and other molecules, causing potential damage or functional changes (Krishnamurthy et al., 2012).

Free radicals also play roles in ion transport across cell membranes, gene expression, and cell signaling, which are essential for cellular communication and regulation (Engwa et al., 2018; Pandey et al., 2010; Naseer et al., 2025). ROS can be generated by normal metabolism, mental stress, intense exercise, or environmental factors like smoking and xenobiotics. Excessive ROS can damage DNA, lipids, and proteins, disrupting cellular function (Jaun et al., 2021).

After fractionation, the methanolic extract of *M. buxifolia* fruit yielded n-hexane, chloroform, ethyl acetate, n-butanol, and aqueous fractions. The highest phenolic and flavonoid contents are found in the n-butanol, aqueous, and methanol fractions. These fractions showed strong antioxidant activity against radicals such as DPPH, ABTS, superoxide, hydroxyl, and hydrogen peroxide, and exhibited significant reducing power in ferric ion and phosphomolybdate assays. Methanol extraction gave the highest yield, while the aqueous fraction yielded the least (Jan et al., 2013).

Anti-Arthritic

Autoimmune disorders occur when the immune system mistakenly attacks the body's own cells and tissues, leading to diseases

like rheumatoid arthritis (RA), a chronic inflammatory condition primarily affecting joints (Reddy et al., 2014). RA causes joint pain, swelling, and destruction of bone and cartilage, potentially resulting in irreversible disability. While its exact causes remain unclear, genetic predisposition and environmental triggers, such as viruses, are believed to contribute (Bubushetty et al., 2012).

RA is characterized by synovial membrane hyperplasia, cartilage damage, and joint degeneration due to inflammation and neovascularization (Chunxia et al., 2011). Autoantibodies often appear in serum and synovial fluid years before symptoms (MacInnes et al., 2011; Mewar et al., 2006). Key processes in RA pathogenesis include protein citrullination, nucleic acid sensing, dysbiosis, and activation of autoreactive T and B cells (Darrah et al., 2018). These pathways trigger transcription factors like NF- κ B and cytokines such as IL-1, IL-6, IL-12, and TNF, promoting inflammation and joint damage (Theofilopoulos et al., 2017; Guo et al., 2018).

M. buxifolia extract (MBME) has been evaluated for anti-arthritis and antioxidant activity after GC-MS characterization. Higher concentrations of MBME increased free radical scavenging, likely due to phenolic and flavonoid content. MBME also stabilized red blood cell membranes in vitro, suggesting it may help stabilize lysosomal membranes and reduce inflammation (Akhtar et al., 2021) (Figure 2, Table 1).

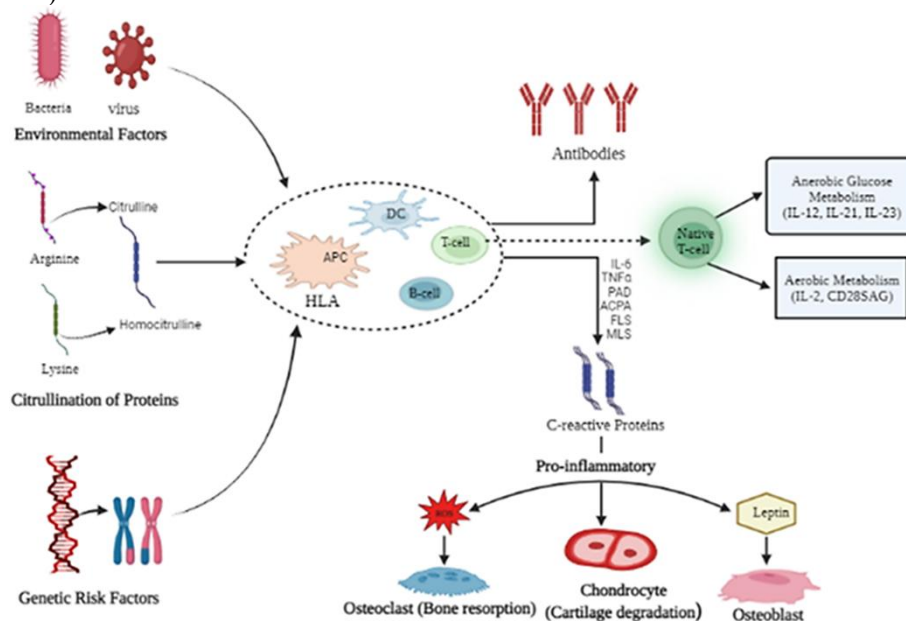


Figure 2: Factors responsible for causing joint deformities.

Antinociceptive and Anti-inflammatory Activity

Antinociceptive activity refers to the ability of a substance to reduce or relieve pain. The International Association for the Study of Pain (IASP) defines pain as the central nervous system's response to tissue injury or emotional disturbances, classifying it as either acute or chronic (Assis et al., 2020). Inflammation is a physiological defense mechanism involving immune cells and mediators that protect against infections, injuries, and harmful substances. Leukocyte and mononuclear phagocyte migration to inflamed sites signals an inflammatory response (Burki et al., 2021; Serhan et al., 2008). Inflammation is closely linked to fatigue and pain transmission (Louati and Berenbaum, 2015; Ambrin et al., 2024).

The Global Pain Index reports that up to 88% of people worldwide experience some form of physical or mental pain, with chronic pain affecting 94% of the population in China (Wen et al., 2023). Lectins, carbohydrate-binding proteins found in many organisms, including plants, can influence pain pathways by modulating voltage-gated calcium channels (Molinski et al., 2009). Plant lectins also show anti-inflammatory, antioxidant, and gastroprotective effects (Konozy et al., 2022).

M. buxifolia has demonstrated significant antinociceptive activity. Studies comparing extracts from its leaves and bark using the acetic acid-induced writhing test and COX-2 inhibition found stronger pain-relief effects from the bark extract, which also reduced paw licking behavior, indicating its potential as a natural analgesic (Burki et al., 2021). Further research confirmed that methanolic bark extract (MBHE) reduced nociception and inflammation in mice models, and led to the isolation of bioactive compounds like oleanolic acid and isoquercetin (Ullah et al., 2016).

Antimicrobial Activity

Infections are primarily caused by microbes such as bacteria, fungi, and parasites. Substances used to kill or inhibit these microbes are called antimicrobials (Javed et al., 2020). Despite advances in antimicrobial drugs, many infectious diseases remain difficult to treat. Since their discovery in 1965, antimicrobial polymers have attracted significant research interest (Ayeleso et al., 2017; Adil et al., 2024).

Scientists continue to explore plant-derived antibacterial compounds like tannins, alkaloids, and flavonoids. *Shigella flexneri* infections cause around 1.5 million deaths annually, mainly through contaminated food and water (Lewis et al., 2006). Fungal infections are a global health challenge, ranging from mild to severe systemic diseases, affecting an estimated 150 million people. *Candida albicans* can cause

serious infections, with candidemia mortality rates reaching up to 50% (Pappas et al., 2006). Additionally, cryptococcal infections cause over 1 million cases yearly in developing countries, resulting in approximately 675,000 deaths (Byrnes et al., 2010). Fungal cell walls, particularly chitin, are primary targets for antifungal drugs (Hu et al., 2007).

The fruit extract of *M. buxifolia* exhibits significant antimicrobial activity against viruses, bacteria, and fungi due to its bioactive compounds such as alkaloids, flavonoids, terpenoids, and phenolic acids. These compounds inhibit pathogens by damaging cell membranes, blocking essential enzymes, disrupting ribosomes, and interfering with DNA synthesis (Naz et al., 2023).

Researchers are also investigating *M. buxifolia* extracts for synthesizing nanoparticles with antimicrobial properties. Silver nanoparticles, in particular, show strong antibacterial effects due to their small size and large surface area, which allow them to penetrate bacterial cell walls, disrupt cellular functions, and ultimately cause cell death (Sirelkhatim et al., 2015; Ali et al., 2020). The antibacterial activity of *M. buxifolia* leaf extract is evaluated using tetrazolium microplates. Atomic force microscopy (AFM) revealed damage to bacterial cells treated with the extract, and PCR is used to amplify bacterial DNA. The tested bacterial strains included *S. epidermidis* ATCC 13518, *S. aureus* ATCC 25923, *P. aeruginosa* ATCC 10145, and *E. coli* ATCC 10536. The extract damaged the cell walls of both gram-positive and gram-negative bacteria, with significant disruption of biofilms around gram-positive strains. DNA decantation is inhibited in *S. aureus* and *S. epidermidis*, but not in *E. coli* or *P. aeruginosa* (Burki et al., 2019).

Traditional uses of *M. buxifolia* fruit are further explored by chemically analyzing various fruit fractions via GC-MS and testing their *vitro* leishmanicidal, antifungal, and antibacterial activities. Compounds identified included hexadecanoic acid, oleic acid, vaccenic acid, and phthalic acid. The extract moderately inhibited the growth of *M. canis* and *F. solani*, with the ethyl acetate fraction showing the strongest antifungal activity (50%) against *F. solani* (Ullah et al., 2019) (Figure 3, Table 1).

Antipyretic Activity

Pyrexia, or fever, is an increase in body temperature caused by infections, hormonal changes, stress, or injuries (Sultana et al., 2015). Antipyretic activity refers to the ability of a substance to reduce fever (Santacorce et al., 2023). Synthetic antipyretics lower fever by blocking COX-2 and prostaglandin synthesis but can harm organs like the liver, brain, and heart. Natural COX-2 blockers tend to have fewer side effects (Niazi et al., 2010).

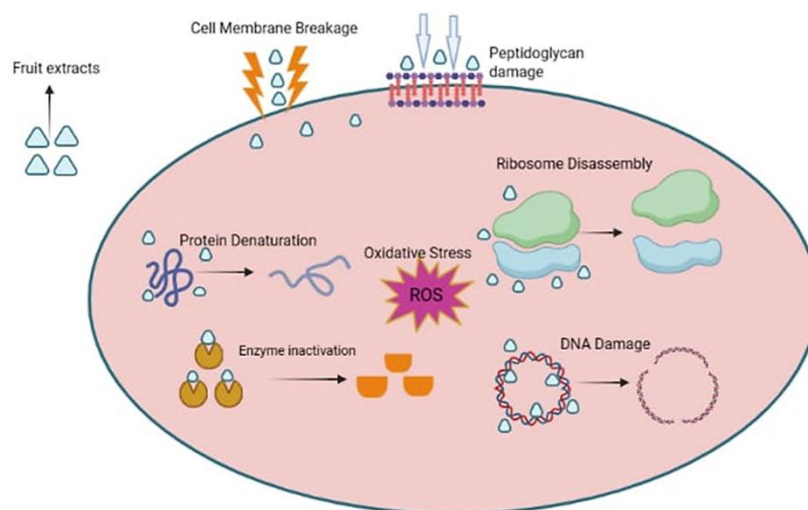


Figure 3: Antimicrobial mechanisms of action of *Monothecha buxifolia* fruit extracts.

M. buxifolia fruit has long been used in traditional medicine for benefits including treating anemia and urinary disorders (Ullah et al., 2016). Analgesics and antipyretics relieve pain and fever by acting on inflammatory mediators like prostaglandins, cytokines, and interleukins (Estella et al., 2022).

In studies, hydro-ethanolic extract of *M. buxifolia* significantly reduced yeast-induced fever in mice, suggesting antipyretic, analgesic, and anti-inflammatory properties likely due to oleanolic acid, isoquercetin, and other phytochemicals (Ullah et al., 2016; Jan et al., 2013).

Heptaprotective Effect

The liver is one of the body's most vital organs, playing a central role in detoxification, bile production, vitamin storage, and the metabolism of fats, proteins, and carbohydrates. Liver disease remains a significant global public health challenge, causing substantial morbidity and mortality worldwide. Many hepatotoxic agents exert their damaging effects through lipid peroxidation and other oxidative injuries to liver cells (Adewusi et al., 2010). Among liver diseases, viral hepatitis is the most prevalent. Hepatitis can result from infections caused by viruses, bacteria, parasites such as amoebas and *Giardia*, as well as from exposure to drugs, toxins, or even certain mushrooms. Liver disorders are estimated to cause approximately 20,000 deaths each year (Bhawna et al., 2009).

Liver diseases are generally categorized into cirrhosis, hepatosis (non-inflammatory disorders), and acute or chronic hepatitis

(inflammatory liver diseases), with cirrhosis involving degenerative changes leading to fibrosis of the liver. Major causes of liver illnesses include toxic chemicals, excessive alcohol consumption, infections, and autoimmune conditions. Notably, around 90% of acute hepatitis cases are attributed to viral infections (Kumar et al., 2011). Hepatotoxic substances often induce lipid peroxidation or oxidative damage in hepatocytes, which can subsequently affect kidney function as well (Haque et al., 2014). Moreover, excessive use of paracetamol (PCM) can cause massive liver cell necrosis, marked by nuclear pyknosis and eosinophilic cytoplasm, leading to severe hepatic injury (Okeyato et al., 2018). The generation of highly reactive trichloromethyl radicals (CCl_3) is another mechanism contributing to liver damage (Minnady et al., 2022).

Numerous medicinal plants have been studied for their hepatoprotective properties. These plants contain diverse bioactive compounds—including phenols, coumarins, lignans, essential oils, xanthenes, alkaloids, monoterpenes, glycosides, carotenoids, organic acids, lipids, and flavonoids—that contribute to their therapeutic potential (Ahmad et al., 2012). The first-line antitubercular medications, isoniazid and rifampicin, are utilized as a standard hepatotoxic in a variety of investigations. The hepatoprotective potential of *M. buxifolia* fruit are investigated using hydro-ethanolic extract against isoniazid and rifampicin. The phytochemical profiling of *M. buxifolia* lead to the isolation of oleanolic acid and isoquercetin. The presence of isoquercetin and oleanolic acid in *M. buxifolia* may have caused it to demonstrate a specific protective effect against the hepatotoxicity caused by isoniazid and rifampicin (Ullah et al., 2016) (Figure 4, Table 1).

Protective Effect of *Monothea Buxifolia* on Renal Toxicity

Globally, 8–16% of people suffer from chronic kidney disease (Jha et al., 2013). The kidneys play a crucial role in regulating mineral metabolism and handling the breakdown and excretion of various substances, making them vulnerable to damage (Komaan et al., 2014; De et al., 2011). Acute kidney injury (AKI) from immune-related adverse events (irAEs) ranges from mild to severe, and drug-induced nephrotoxicity contributes to over 60% of AKI cases. In the US, drug-induced nephrotoxicity affects about 20% of adults and causes 1.5 million adverse events annually (Sesi et al., 2019; Mukharjee et al., 2022; Davis et al., 2016). Causes include crystal nephropathy, inflammation, tubular toxicity, thrombotic microangiopathy, and altered glomerular hemodynamics (Schetz et al., 2005). Podocyte injury disrupts the glomerular filtration barrier, leading to nephrotic syndrome (Paukesakon et al., 2017; Srivastava et al., 2021). Acute interstitial nephritis (AIN) can

result from drugs like antibiotics, phenytoin, proton pump inhibitors, and lithium, causing immune-mediated inflammation (Moledina et al., 2017).

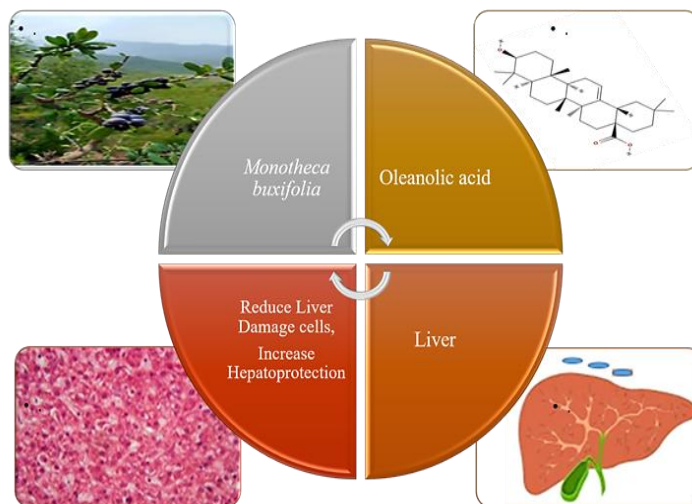


Figure 4: Effect of *Monothecha buxifolia* on hepatoprotection.

Antimalarial Activity

Malaria, caused by *Plasmodium* species transmitted by female *Anopheles* mosquitoes, remains a major global health issue, with 241 million cases and 627,000 deaths reported in 2020 (Okokon et al., 2022). During its erythrocytic stage, *Plasmodium* consumes 60–80% of hemoglobin in red blood cells, producing ferriprotoporphyrin IX, which is toxic to the parasite (Acosta et al., 2022).

Plant compounds like alkaloids, terpenes, steroids, and flavonoids exhibit antimalarial activity (T.N.C. et al., 2011). *M. buxifolia* leaves contain cardiac glycosides, flavonoids, tannins, anthraquinones, saponins, terpenoids, and reducing sugars (Nawaz et al., 2019). A methanolic extract of *M. buxifolia* showed significant inhibition (up to 80–82%) against *Plasmodium vivax* and *P. falciparum* in human blood samples (Din et al., 2018). Members of the Sapotaceae family, including *M. buxifolia*, have demonstrated effective antimalarial activity (Adewoye et al., 2010).

Free radicals cause lipid peroxidation, damaging kidney cell membranes and leading to renal disease (Jan et al., 2016). Prompt treatment is essential to maintain blood flow and prevent progression to end-stage renal disease or death (Yu et al., 2022). *M. buxifolia* fruit, known locally as Gurguray, contains high levels of phenolics and flavonoids and exhibits strong antioxidant, iron-chelating, and free radical-scavenging

activities, suggesting potential protective effects on renal health (Rehman et al., 2013; Farid et al., 2012) (Figure 5, Table 1).

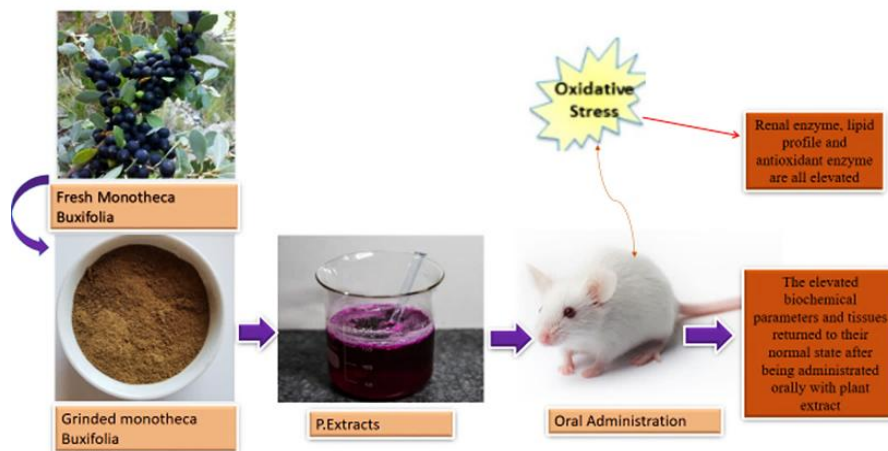


Figure 5: *Monothecha buxifolia* protective effects against kidney toxicity.

Plant extracts, such as MBM, which include dietary polyphenols, have been shown to have the ability to protect against kidney damage caused by harmful compounds, such as carbon tetrachloride. This is identified via research conducted by scientists. (CCl₄). According to the findings of study that is carried out not too long ago, MBM is shown to have protective effects that are equivalent to those of CCl₄ in preventing kidney injury in rats. According to the results of the study, giving MBM to rats helped restore their renal function and significantly raised the levels of phase II antioxidant enzymes in their bodies (Javed et al., 2021).

Phytochemistry of *Monothecha buxifolia*

Many natural compounds have been developed into modern medicines. Plants produce secondary metabolites that support their survival and reproduction (Agdew et al., 2022). The leaves of *M. buxifolia* contain polyphenols, anthraquinones, terpenoids, saponins, reducing sugars, tannins, and flavonoids, with flavonoids and polyphenols showing strong analgesic and anti-inflammatory effects (Murad et al., 2013). Key phytochemicals identified in *M. buxifolia* include lauric acid, oleanolic acid, and bis(2-ethylhexyl) phthalate (Hassan et al., 2018).

Phytochemical screening revealed that methanol and chloroform extracts of *M. buxifolia* fruit contain flavonoids, terpenoids, tannins, saponins, anthraquinones, and cardiac glycosides. Flavonoids, terpenoids, and saponins are consistently found in fruit pulp extracts across various

solvents (Ali et al., 2022). Flavonoids are widely used in cosmetics, nutraceuticals, and pharmaceuticals due to their antioxidant, anti-inflammatory, anti-mutagenic, and anti-carcinogenic properties (Panche et al., 2016). They help protect against chronic diseases such as cancer, Alzheimer's, and atherosclerosis, earning them recognition as "functional components" and health-promoting biomolecules (Karak et al., 2019). Many flavonoids, including apigenin, galangin, flavones, flavonol glycosides, isoflavones, flavanones, and chalcones, also show strong antibacterial activity (Kumar et al., 2013) (Figure 6, Table 1).

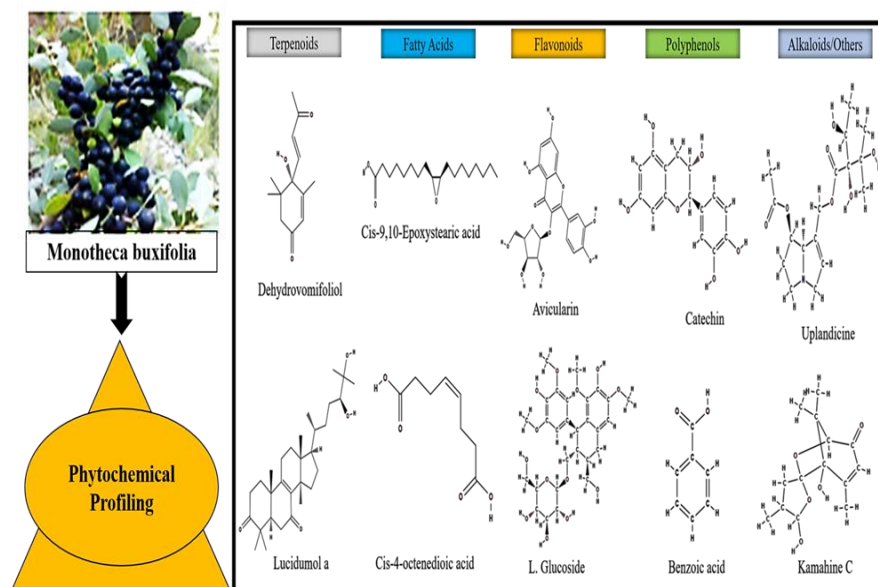


Figure 6: Phytochemistry of *Monotheca buxifolia*.

Flavonoids are best known for their antioxidant properties but also show anti-inflammatory, vasodilatory, anticoagulant, cardioprotective, antidiabetic, neuroprotective, and anti-obesity effects (Fan et al., 2022). Flavonoids like fisetin and luteolin exhibit anti-aging properties and help eliminate senescent cells, supporting their use in anti-aging treatments (Yousafzadeh et al., 2018).

Alkaloids are nitrogen-containing compounds found in about 20% of plant species, with over 5,500 known types (Roy et al., 2017). Despite their toxicity, plants use them for defense. Alkaloids also possess hepatoprotective, anti-inflammatory, antispasmodic, and other therapeutic properties (Nguyen et al., 2022). Quaternary alkaloids such as palmatine and tetrahydropalmatine have shown antimalarial effects in vitro (Birbi et al., 2018).

Terpenoids, derived from mevalonic acid and composed of isoprene units, number over 50,000 identified compounds in nature. They support transdermal drug delivery, help manage cardiovascular diseases, lower blood sugar, and act as insecticides, antioxidants, and neuroprotectants (George et al., 2015). For example, stevioside from *Stevia rebaudiana* improves energy metabolism and may help prevent insulin resistance (Jeppesen et al., 2006).

Saponins, named for their soap-like foaming in water, can lower cholesterol, prevent cancer, and modulate immunity (Azimova et al., 2013; Marelli et al., 2016). Anthraquinones, a type of polyketide produced by fungi, may aid wound healing and reduce cancer risk (Malik et al., 2016; Sebak et al., 2022).

Conclusion

Natural products have been used as medicinal agents for many years. In the current perspective, natural products have provided and will continue to provide a special aspect of molecular diversity and biological activity in therapeutic research and development. *M. buxifolia* is promising medical plant with diverse pharmacological activities. The phytochemical constituents of the plant, including flavonoids, alkaloids, saponins, terpenoids, and anthraquinones contribute to its therapeutic agent potential. The subject of this reviews is the phytochemistry, pharmacological application of plant *M. buxifolia*. This is an effort to assemble and document information on different features of the plant and highlight the requirement for research and development. Further research is needed to fully elucidate the mechanisms of action of these phytochemicals and to develop effective and safe herbal medicine from this plant.

Conflicts of Interest

The authors declare no conflict of interest.

References

- Acosta, M. E., Gotopo, L., Gamboa, N., Rodrigues, J. R., Henriques, G. C., Cabrera, G., & Romero, A. H. (2022). Antimalarial Activity of Highly Coordinative Fused Heterocycles Targeting β -Hematin Crystallization. *ACS omega*, 7(9), 7499-7514.
- Adewoye, E. O., Salami, A. T., & Taiwo, V. O. (2010). Anti-plasmodial and toxicological effects of methanolic bark extract of *Chrysophyllum albidum* in albino mice. *Journal of Physiology and Pathophysiology*, 1(1), 1-9

- Adewusi, E. A., & Afolayan, A. J. (2010). A review of natural products with hepatoprotective activity. *Journal of Medicinal Plants Research*, 4(13), 1318-1334.
- Adil, M., Dastagir, G., Quddoos, A., Naseer, M., & Filimban, F. Z. (2024). HPLC analysis, genotoxic and antioxidant potential of *Achillea millefolium* L. and *Chaerophyllum villosum* Wall ex. Dc. *BMC Complementary Medicine and Therapies*, 24(1), 91.
- Adil, M., Filimban, F. Z., Ambrin, Quddoos, A., Sher, A. A., & Naseer, M. (2024). Phytochemical screening, HPLC analysis, antimicrobial and antioxidant effect of *Euphorbia parviflora* L. (Euphorbiaceae Juss.). *Scientific Reports*, 14(1), 5627.
- Agidew, M. G. (2022). Phytochemical analysis of some selected traditional medicinal plants in Ethiopia. *Bulletin of the National Research Centre*, 46(1), 1-22.
- Ahmed, M., Hegde, S. V., Chavan, A., Lakshmikantha, R. Y., & Thimmappanahalli, K. B. (2012). Evaluation of hepatoprotective activity of *Vitis vinifera* stem bark. *Journal of Pharmacy Research*, 5(11), 5228-5230.
- Akhtar, M. F., Khan, K., Saleem, A., Baig, M. M. F. A., Rasul, A., & Abdel-Daim, M. M. (2021). Chemical characterization and anti-arthritis appraisal of *Monothea buxifolia* methanolic extract in Complete Freund's Adjuvant-induced arthritis in Wistar rats. *Inflammopharmacology*, 29, 393-408.
- Akhtar, N., & Mirza, B. (2018). Phytochemical analysis and comprehensive evaluation of antimicrobial and antioxidant properties of 61 medicinal plant species. *Arabian journal of chemistry*, 11(8), 1223-1235.
- Ali, A. H., Ahmed, H. S., Jawad, A. S., & Mustafa, M. A. (2021). Endorphin: function and mechanism of action. *Sci Arch*, 2, 9-13.
- Ali, F., Khan, N., & Rahmonov, O. (2022). Ecosystem Services and Linkages of Naturally Managed *Monothea buxifolia* (Falc.) A. DC. Forests with Local Communities across Contiguous Mountainous Ranges in Pakistan. *Biology*, 11(10), 1469.
- Ali, F., Khan, N., Khan, A. M., Ali, K., & Abbas, F. (2023). Species distribution modelling of *Monothea buxifolia* (Falc.) A. DC.: Present distribution and impacts of potential climate change. *Heliyon*, 9(2).
- Ali, J. S., Mannan, A., Nasrullah, M., Ishtiaq, H., Naz, S., & Zia, M. (2020). Antimicrobial, antioxidative, and cytotoxic properties of *Monothea buxifolia* assisted synthesized metal and metal oxide nanoparticles. *Inorganic and Nano-Metal Chemistry*, 50(9), 770-782.

- Ambrin, A., Adil, M., Filimban, F. Z., & Naseer, M. (2024). Chemical Profiling and Biological Activities of *Ziziphus Mauritiana* var. *spontanea* (Edgew.) RR Stewart ex Qaiser & Nazim. and *Oenothera Biennis* L. *Journal of Food Quality*, 2024(1), 7318407.
- Aneszweski, T. (2007). *Alkaloids-Secrets of Life: Alkaloid Chemistry, Biological Significance, Applications and Ecological Role*. Elsevier.
- Assis, D. B., Aragao Neto, H. D. C., da Fonsêca, D. V., de Andrade, H. H. N., Braga, R. M., Badr, N., & de Almeida, R. N. (2020). Antinociceptive activity of chemical components of essential oils that involves docking studies: a review. *Frontiers in pharmacology*, 11, 777.
- Ayeleso, T. B., Matumba, M. G., & Mukwevho, E. (2017). Oleanolic acid and its derivatives: biological activities and therapeutic potential in chronic diseases. *Molecules*, 22(11), 1915.
- Azimova, S. S., & Yunusov, M. S. (Eds.). (2013). *Natural Compounds: Alkaloids* (pp. 02-04). Springer New York.
- Babushetty, V., & Sultanpur, M. C. (2012). Evaluation of anti-arthritis activity of *Asystasia dalzelliana* leaves. *International Journal of Pharmacology Biol Arch*, 3(2), 377-382.
- Bhawna, S., & Kumar, S. U. (2009). Hepatoprotective activity of some indigenous plants. *International Journal of Pharmacy and Technology Research*, 4, 1330-1334.
- Bongomin, F., Gago, S., Oladele, R. O., & Denning, D. W. (2017). Global and multi-national prevalence of fungal diseases—estimate precision. *Journal of fungi*, 3(4), 57.
- Bribi, N. (2018). Pharmacological activity of alkaloids: a review. *Asian journal of botany*, 1(1), 1-6.
- Burki, S., Asghar, M. A., Burki, Z. G., & Rehman, A. A. (2021). Anti-nociceptive and Anti-inflammatory Effect of *Monothea buxifolia* Leaves and Bark Extract: A Comparative Approach. *RADS Journal of Pharmacy and Pharmaceutical Sciences*, 9(2), 115-123.
- Burki, S., Burki, Z. G., Jahan, N., Muhammad, S., Mohani, N., Siddiqui, F. A., & Owais, F. (2019). GC-MS profiling, FTIR, metal analysis, antibacterial and anticancer potential of *Monothea buxifolia* (Falc.) leaves. *Pakistan Journal of Pharmaceutical Sciences*, 32.
- Byrnes III, E. J., Li, W., Lewit, Y., Ma, H., Voelz, K., Ren, P., & Heitman, J. (2010). Emergence and pathogenicity of highly virulent *Cryptococcus gattii* genotypes in the northwest United States. *PLoS pathogens*, 6(4), e1000850.

- Chunxia, C., Peng, Z., Huifang, P., Hanli, R., Zehua, H., & Jizhou, W. (2011). Extracts of *Arisaema rhizomatum* CEC Fischer attenuate inflammatory response on collagen-induced arthritis in BALB/c mice. *Journal of Ethnopharmacology*, 133(2), 573-582.
- Cyran, A. M., & Zhitkovich, A. (2022). HIF1, HSF1, and NRF2: Oxidant-Responsive Trio Raising Cellular Defenses and Engaging Immune System. *Chemical research in toxicology*, 35(10), 1690-1700.
- Darrah E, Andrade F. Rheumatoid arthritis and citrullination. *Curr Opin Rheumatol*. 2018; 30(1):72-78.
- Davis-Ajami, M. L., Fink, J. C., & Wu, J. (2016). Nephrotoxic medication exposure in US adults with predialysis chronic kidney disease: health services utilization and cost outcomes. *Journal of Managed Care & Specialty Pharmacy*, 22(8), 959-968.
- De Oliveira, R. B., De Paula, D. A. C., Rocha, B. A., Franco, J. J., Gobbo-Neto, L., Uyemura, S. A., ... & Da Costa, F. B. (2011). Renal toxicity caused by oral use of medicinal plants: the yacon example. *Journal of ethnopharmacology*, 133(2), 434-441.
- Debnath, B., Singh, W. S., Das, M., Goswami, S., Singh, M. K., Maiti, D., & Manna, K. (2018). Role of plant alkaloids on human health: A review of biological activities. *Materials today chemistry*, 9, 56-72.
- Engwa, G. A. (2018). Free radicals and the role of plant phytochemicals as antioxidants against oxidative stress-related diseases. *Phytochemicals: Source of Antioxidants and Role in Disease Prevention. BoD—Books on Demand*, 7, 49-74.
- Estella, O. U., William, A. C., Patrick, O., Ikenna, C., Mba, T., Obinna, O., & Ginikachukwu, U. (2022). Evaluation of the analgesic and antipyretic activity of methanol extract of *Combretum bauchiense* Hutch & Dalziel (Combretaceae) leaves. *Phytomedicine Plus*, 2(1), 100166.
- Fan, X., Fan, Z., Yang, Z., Huang, T., Tong, Y., Yang, D. & Yang, M. (2022). Flavonoids—Natural gifts to promote health and longevity. *International Journal of Molecular Sciences*, 23(4), 2176.
- Farid S, Khan IU, Rehman J. In-vitro evaluation of antioxidant activity of *Monothea buxifolia*: A spectrophotometric approach. Amazon: LAP LAMBERT Academic Publishing; 2012. p. 1–80.
- George, K. W., Alonso-Gutierrez, J., Keasling, J. D., & Lee, T. S. (2015). Isoprenoid drugs, biofuels, and chemicals—artemisinin, farnesene, and beyond. *Biotechnology of isoprenoids*, 355-389.

- Guo Q, Wang Y, Xu D, Nossent J, Pavlos NJ, Xu J. Rheumatoid arthritis: pathological mechanisms and modern pharmacologic therapies. *Bone research*. 2018; 6:15.
- Halliwell, B. (2007). Biochemistry of oxidative stress. *Biochemical society transactions*, 35(5), 1147-1150.
- Haque, A., Tahmina, A. S., Sarker, I. R., Hossain, M., Islam, S., & Islam, A. (2014). Antioxidant and hepatoprotective effects of aqueous and ethanol extracts of *Dendrophthoe falcate* Linn leaves. *Archives*, 1, 90-101.
- Hassan, S. (2018). *PHYTOCHEMICAL, ETHNOMEDICINAL AND BIOASSAY SCREENING OF AERIAL PARTS OF MONOTHECA BUXIFOLIA AND BOSEA AMHERSTIANA* (Doctoral dissertation, University of Peshawar).
- Hassan, S., Ahmad, B., Khan, S. U., Linfang, H., Anjum, S. I., Ansari, M. J., ... & Shah, A. H. (2019). In vivo pharmacological investigation of *Monothea buxifolia* and *Bosea amherstiana* using animal models. *Saudi Journal of Biological Sciences*, 26(7), 1602-1606.
- Hu, Y., Zhang, J., Kong, W., Zhao, G., & Yang, M. (2017). Mechanisms of antifungal and anti-aflatoxigenic properties of essential oil derived from turmeric (*Curcuma longa* L.) on *Aspergillus flavus*. *Food chemistry*, 220, 1-8.
- Jan, S., & Khan, M. R. (2016). Protective effects of *Monothea buxifolia* fruit on renal toxicity induced by CCl₄ in rats. *BMC complementary and alternative medicine*, 16, 1-15.
- Jan, S., Khan, M. R., Rashid, U., & Bokhari, J. (2013). Assessment of antioxidant potential, total phenolics and flavonoids of different solvent fractions of *Monothea buxifolia* fruit. *Osong public health and research perspectives*, 4(5), 246-254.
- Jan, S., Khan, M. R., Rashid, U., & Bokhari, J. (2013). Assessment of antioxidant potential, total phenolics and flavonoids of different solvent fractions of *Monothea buxifolia* fruit. *Osong public health and research perspectives*, 4(5), 246-254.
- Javed, R., Zia, M., Naz, S., Aisida, S. O., Ain, N. U., & Ao, Q. (2020). Role of capping agents in the application of nanoparticles in biomedicine and environmental remediation: recent trends and future prospects. *Journal of Nanobiotechnology*, 18, 1-15.
- Javed, S., Shoaib, A., Mahmood, Z., & Ishtiaq, S. (2021). Hepatoprotective effect of methanolic extract of *Monothea buxifolia* against isoniazid and rifampicin induced hepatotoxicity. *Asian Journal of Agriculture and Biology*, 3.
- Jeppesen, P. B., Rolfsen, S. E., Agger, A., Gregersen, S., Colombo, M., Xiao, J., & Hermansen, K. (2006). Can stevioside in combination

- with a soy-based dietary supplement be a new useful treatment of type 2 diabetes? An in vivo study in the diabetic goto-kakizaki rat. *The Review of Diabetic Studies: RDS*, 3(4), 189.
- Jha, V.; Garcia-Garcia, G.; Iseki, K.; Li, Z.; Naicker, S.; Plattner, B.; Saran, R.; Wang, A.Y.; Yang, C.W. Chronic kidney disease: Global dimension and perspectives. *Lancet* 2013, 382, 260–272.
- Juan, C. A., Pérez de la Lastra, J. M., Plou, F. J., & Pérez-Lebeña, E. (2021). The chemistry of reactive oxygen species (ROS) revisited: outlining their role in biological macromolecules (DNA, lipids and proteins) and induced pathologies. *International Journal of Molecular Sciences*, 22(9), 4642.
- Karak, P. (2019). Biological activities of flavonoids: an overview. *Int. J. Pharm. Sci. Res*, 10(4), 1567-1574.
- Khayti, S., Gaboun, F., Pirro, S., Tatusova, T., El Mousadik, A., Ghazal, H., & Mentag, R. (2020). Complete chloroplast genome of *Argania spinosa*: Structural organization and phylogenetic relationships in Sapotaceae. *Plants*, 9(10), 1354.
- Konozy, E. H. E., Osman, M. E. F. M., & Dirar, A. I. (2022). Plant lectins as potent Anti-coronaviruses, Anti-inflammatory, antinociceptive and antiulcer agents. *Saudi Journal of Biological Sciences*, 103301.
- Kooman JP, Kotanko P, Schols A et al. Chronic kidney disease and premature ageing. *Nat Rev Nephrol* 2014; 10: 732–74.
- Krishnamurthy P, Wadhwani A. Antioxidant enzymes and human health. In: El-Missiry MA, editor. *Antioxidant Enzyme*. Croatia: In Tech; 2012. pp. 3-18.
- Kumar, C. H., Ramesh, A., Kumar, J. S., & Ishaq, B. M. (2011). A review on hepatoprotective activity of medicinal plants. *International journal of Pharmacology*.
- Kumar, S., & Pandey, A. K. (2013). Chemistry and biological activities of flavonoids: an overview. *The scientific world journal*, 2013.
- Lewis, K. & Ausubel, F.M., Prospects for Plant-Derived Antibacterial, *Nature Biotechnology*, 24(12), pp. 1504-1507, 2006.
- Louati, K., & Berenbaum, F. (2015). Fatigue in chronic inflammation-a link to pain pathways. *Arthritis research & therapy*, 17(1), 1-10.
- Malik, E. M., & Müller, C. E. (2016). Anthraquinones as pharmacological tools and drugs. *Medicinal research reviews*, 36(4), 705-748.
- Marrelli, M., Conforti, F., Araniti, F., & Statti, G. A. (2016). Effects of saponins on lipid metabolism: A review of potential health benefits in the treatment of obesity. *Molecules*, 21(10), 1404.
- McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. *New England Journal of Medicine*. 2011; 365(23):2205-2219.

- Mewar D, Wilson AG. Autoantibodies in rheumatoid arthritis: a review. *Biomedicine & pharmacotherapy* = *Biomedicine & pharmacotherapies*. 2006; 60(10):648-655.
- Minnady, M., Jayapal, G., Poochi, S., Nethaji, P., & Mathalaimuthu, B. (2022). Hepatoprotective Effect of Indigenous Medicinal Plants- A Review. *Indian Journal of Pharmaceutical Sciences*, 84(5), 1116-1132.
- Moledina, D. G., & Perazella, M. A. (2017). Drug-induced acute interstitial nephritis. *Clinical Journal of the American Society of Nephrology*, 12(12), 2046-2049.
- Moliniski TF, Dalisay DS, Lievens SL, Saludes JP. Drug development from marine natural products. *Nat Rev Drug Discov*. 2009; 8(1):69-85.
- Mueller I, Zimmerman PA, Reeder JC. 2007. *Plasmodium malariae* and *Plasmodium ovale*: The "bashful" malaria parasites. *Trends in Parasitology* 23, 278-83
- Mukherjee, K.; Chio, T.I.; Gu, H.; Sackett, D.L.; Bane, S.L.; Sever, S. A Novel Fluorogenic Assay for the Detection of Nephrotoxin-Induced Oxidative Stress in Live Cells and Renal Tissue. *ACS Sens*. 2021, 6, 2523–2528.
- Murad, W., Azizullah, A., Adnan, M., Tariq, A., Khan, K. U., Waheed, S., & Ahmad, A. (2013). Ethnobotanical assessment of plant resources of Banda Daud Shah, district Karak, Pakistan. *Journal of ethnobiology and ethnomedicine*, 9, 1-10.
- Naseer, M., Adil, M., Ahmad, S., Almutairi, M. H., Alrefaei, A. F., Ali, S., & Asad, F. (2025). Gas Chromatography-Mass Spectrometry Analysis, Genoprotective, and Antioxidant Potential of *Curio Radicans* (L. f.) PV Heath. *ChemistryOpen*, 2500175.
- Nawaz, F., Ahmad, S., Naheed, S., Ahmad, Z., & Mehmmod, T. (2019). Phytochemical screening by FTIR spectroscopic analysis of leaf extracts of *Monothea buxifolia*. *University of Wah Journal of Science and Technology (UWJST)*, 3, 15-22.
- Naz, S., Gul, A., Zia, M., & Javed, R. (2023). Synthesis, biomedical applications, and toxicity of Santacorce, L., Colella, M., Charitos, I. A., Di Domenico, M., Palmirotta, R., & Jirillo, E. (2023). Microbial and Host Metabolites at the Backstage of Fever: Current Knowledge about the Co-Ordinate Action of Receptors and Molecules Underlying Pathophysiology and Clinical Implications. *Metabolites*, 13(3), 461.
- CuO nanoparticles. *Applied Microbiology and Biotechnology*, 1-23.
- Nguyen, L. H., Vo, V. T., Le Tuan, M. T., Vo, T. P., Le Tan, N. T., & Nguyen, D. Q. (2022). Hydro-alcoholic Extraction by an

- Ultrasound Assisted Leaching Method of *Crotalaria assamica* Benth Seed Powder for Pharmaceutical Purposes: Optimization using RSM and Basic Properties. *Chemical Engineering Transactions*, 97, 103-108.
- Niazi, J., Gupta, V., Chakarborty, P., & Kumar, P. (2010). Anti-inflammatory and antipyretic activity of *Aleuritis moluccana* leaves. *Asian J Pharm Clin Res*, 3(1), 35-37.
- Okaiyeto, K., Nwodo, U., Mabinya, L., & Okoh, A. (2018). A review on some medicinal plants with hepatoprotective effects. *Pharmacognosy Reviews*, 12(24), 186-199.
- Okokon, J. E., Mobley, R., Edem, U. A., Bassey, A. I., Fadayomi, I., Drijfhout, F., & Li, W. W. (2022). In vitro and in vivo antimalarial activity and chemical profiling of sugarcane leaves. *Scientific Reports*, 12(1), 1-13.
- Panche, A. N., Diwan, A. D., & Chandra, S. R. (2016). Flavonoids: an overview. *Journal of nutritional science*, 5, e47.
- Pandey KB, Rizvi SI. Markers of oxidative stress in erythrocytes and plasma during aging in humans. *Oxidative Medicine and Cellular Longevity*. 2010; 3(1):2-12
- Pappas, P.G. Invasive Candidiasis. *Infect. Dis. Clin. North Am.* 2006, 20, 485–506.
- Patel, V., Gandhi, D., Patel, H., & Acharya, N. (2023). Potential of Herbal Drugs for Treatment of Tuberculosis. In *Tubercular Drug Delivery Systems: Advances in Treatment of Infectious Diseases* (pp. 307-333). Cham: Springer International Publishing.
- Paueksakon, P.; Fogo, A.B. Drug-induced nephropathies. *Histopathology* 2017, 70, 94–108.
- Rai, S., & Kumar, A. (2022). Bacteriophage therapeutics to confront multidrug-resistant *Acinetobacter baumannii*-a global health menace. *Environmental microbiology reports*, 14(3), 347-364.
- Rajasree, R. S., Sibi, P. I., Francis, F., & William, H. (2016). Phytochemicals of Cucurbitaceae family—A review. *International Journal of Pharmacognosy and Phytochemical Research*, 8(1), 113-123.
- Raut, J. S., & Karuppayil, S. M. (2014). A status review on the medicinal properties of essential oils. *Industrial crops and products*, 62, 250-264.
- Reddy, V. J. S., Rao, P. G. D., & Lakshmi, G. R. (2014). A review on antiarthritic activity of some medicinal plants. *J Glob Trends Pharm Sci*, 5(4), 2061-73.
- Rehman, J., Khan, I. U., Farid, S., Kamal, S., & Aslam, N. (2013). Phytochemical screening and evaluation of in-vitro antioxidant

- potential of *Monothea buxifolia*. *E3 J. Biotechnology. Pharmacological. Research*, 4(4), 54-60.
- Roy, A. (2017). A review on the alkaloids an important therapeutic compound from plants. *IJPB*, 3(2), 1-9.
- Schetz, M.; Dasta, J.; Goldstein, S.; Golper, T. Drug-induced acute kidney injury. *Curr. Opin. Crit. Care* 2005, 11, 555–565.
- Sebak, M., Molham, F., Greco, C., Tammam, M. A., Sobeh, M., & El-Demerdash, A. (2022). Chemical diversity, medicinal potentialities, biosynthesis, and pharmacokinetics of anthraquinones and their congeners derived from marine fungi: a comprehensive update. *RSC advances*, 12(38), 24887-24921.
- Serhan, C. N., Chiang, N., & Van Dyke, T. E. (2008). Resolving inflammation: dual anti-inflammatory and pro-resolution lipid mediators. *Nature Reviews Immunology*, 8(5), 349-361.
- Shakya, A. K. (2016). Medicinal plants: Future source of new drugs. *International Journal of Herbal Medicine*, 4(4), 59-64.
- Sirelkhatim, A., Mahmud, S., Seeni, A., Kaus, N. H. M., Ann, L. C., Bakhori, S. K. M., & Mohamad, D. (2015). Review on zinc oxide nanoparticles: antibacterial activity and toxicity mechanism. *Nano-micro letters*, 7, 219-242.
- Sise, M. E., Seethapathy, H., & Reynolds, K. L. (2019). Diagnosis and management of immune checkpoint inhibitor-associated renal toxicity: illustrative case and review. *The Oncologist*, 24(6), 735-742.
- Srivastava, T., Heruth, D. P., Duncan, R. S., Rezaiekhalthigh, M. H., Garola, R. E., Priya, L. Sharma, M. (2021). Transcription factor β -catenin plays a key role in fluid flow shear stress-mediated glomerular injury in solitary kidney. *Cells*, 10(5), 1253.
- Storniolo, A.; Raciti, M.; Cucina, A.; Bizzarri, M.; Di Renzo, L. Quercetin affects Hsp70/IRE1 α mediated protection from death induced by endoplasmic reticulum stress. *Oxidative Med. Cell. Longev.* 2015, 2015, 645157.
- Sultana, S., Asif, H. M., Akhtar, N., & Ahmad, K. (2015). Medicinal plants with potential antipyretic activity: A review. *Asian Pacific Journal of Tropical Disease*, 5, S202-S208.
- SUN, L. C., LI, S. Y., WANG, F. Z., & XIN, F. J. (2017). Research progresses in the synthetic biology of terpenoids. *Biotechnology Bulletin*, 33(1), 64.
- T. N. C. Wells, "Natural products as starting points for future anti-malarial therapies: going back to our roots?" *Malaria Journal*, vol. 10, no. S1, 2011.

- Terra-Araujo, M. H., de Faria, A. D., Vicentini, A., Nylinder, S., & Swenson, U. (2015). Species tree phylogeny and biogeography of the Neotropical genus *Pradosia* (Sapotaceae, Chrysophylloideae). *Molecular Phylogenetics and Evolution*, 87, 1-13
- Thakur, N., Das, S., & Mondal, B. (2020). Occurrence of Diseases of Medicinal and Aromatic Plants in Homestead Garden under Red and Lateritic Zone of West Bengal. *Int. J. Curr. Microbiol. App. Sci*, 9(12), 1809-1817.
- Theofilopoulos AN, Kono DH, Baccala R. The multiple pathways to autoimmunity. *Nature immunology*. 2017; 18(7):716-724.
- Ullah, I., Khan, J. A., Adhikari, A., & Shahid, M. (2016). Hepatoprotective effect of *Monothea buxifolia* fruit against antitubercular drugs-induced hepatotoxicity in rats *Pharmacology*||, 11(1), 248-256.
- Uritu, C. M., Mihai, C. T., Stanciu, G. D., Dodi, G., Alexa-Stratulat, T., Luca, A., & Tamba, B. I. (2018). Medicinal plants of the family Lamiaceae in pain therapy: A review. *Pain Research and Management*, 2018
- Wen, Y., Wang, Z., Zhang, R., Zhu, Y., Lin, G., Li, R., & Zhang, J. (2023). The antinociceptive activity and mechanism of action of cannabigerol. *Biomedicine & Pharmacotherapy*, 158, 114163.
- Xie, J. T., Shao, Z. H., Hoek, T. L. V., Chang, W. T., Li, J., Mehendale, S. & Yuan, C. S. (2006). Antioxidant effects of ginsenoside Re in cardiomyocytes. *European journal of pharmacology*, 532(3), 201-207.
- Yang, W., Chen, X., Li, Y., Guo, S., Wang, Z., & Yu, X. (2020). Advances in pharmacological activities of terpenoids. *Natural Product Communications*, 15(3), 1934578X20903555.
- Yang, W., Chen, X., Li, Y., Guo, S., Wang, Z., & Yu, X. (2020). Advances in pharmacological activities of terpenoids. *Natural Product Communications*, 15(3), 1934578X20903555
- Yousafzadeh, M.; Zhu, Y.; McGowan, S.; Angelini, L.; Fuhrmann-Stroissnigg, H.; Xu, M.; Ling, Y.; Melos, K.; Pirtskhalava, T.; Inman, C.; et al. Fisetin is a senotherapeutic that extends health and lifespan. *Biomedicine* 2018, 36, 18–28.
- Yu, P., Duan, Z., Liu, S., Pachon, I., Ma, J., Hemstreet, G. P., & Zhang, Y. (2022). Drug-induced nephrotoxicity assessment in 3D cellular models. *Micromachines*, 13(1), 3.