Research Article

Drugs Discovery from Traditional Phytotherapy

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Background. Phytotherapy refers to the use of plant extracts for therapeutic purpose. It plays important role in ancient medicine practices. It has been considered as a cornerstone in the development of modern drugs. With the advancement in the field of science and technology, researchers systematically evaluate the medicinal properties of plants.

Objective. It is an integrative approach that integrates traditional knowledge with modern techniques for identification, isolation, and test for plant derivative compounds. Literature on plant-derived natural products used as suitable precursors for drug discovery and development was included.

Methods. The data on plant-derived natural products used as a source for drug discovery and development were obtained through literature publications using different scientific literature and search engines.

Results. These papers were carefully evaluated, critically analyzed and structured with accurate information. The process begins with ethnobotanical surveys and the study of traditional medicine to select promising therapeutic potential herb. Phytochemical methods are then employed to extract and isolate the active constituents. The phytotherapy drugs have the natural properties of plants to support health and manage various conditions. Recently in analytical chemistry and genomics have been essential in accelerating the drug discovery process. High-throughput screening, molecular docking, and bioinformatics tools have enabled the rapid identification of bioactive compounds. Traditional phytotherapy has significantly influenced modern medicine by providing a wealth of knowledge about plant-based remedies. Many pharmaceuticals have roots in herbal practices, with compounds isolated from plants forming the basis for effective treatments.

Conclusion. This integration of traditional wisdom with scientific research has led to the development of targeted therapies, emphasizing the importance of natural products in drug discovery. As researchers continue to explore plant compounds, traditional phytotherapy remains a vital source for potential new medicines. Moreover, advancements in pharmacokinetics and pharmacodynamics have

improved understanding of plant compounds interact with biological systems, enhancing their therapeutic efficacy and safety profiles.

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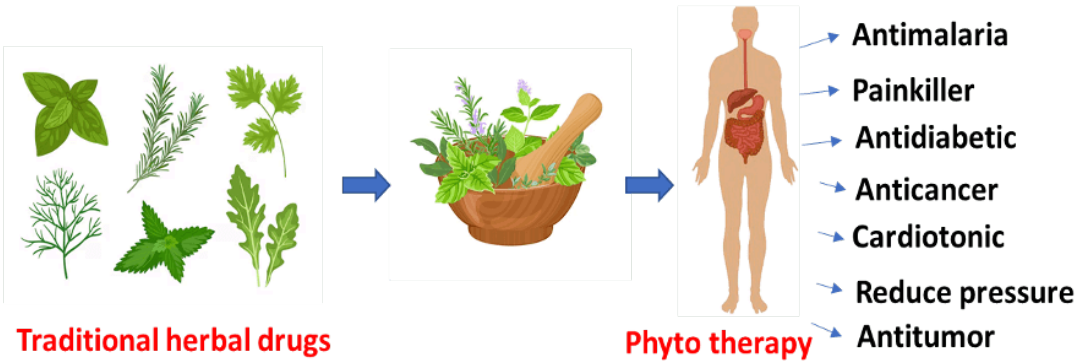

1. Introduction

Herbal phytotherapy is the science and application of medicinal plants and their extracts for medical purposes. The molecules within these plants, known as phytochemicals, have a variety of biological effects and activities and are the foundation of many essential and modern synthetic pharmaceuticals[1]. The discovery of drugs from herbal phytotherapy, also known as plant-based medicine, is a diverse and exciting subject that unites botany, chemistry, pharmacology, and medicine[2]. This is a critically important component of human health and well-being, and humanity has been practicing the use of medicinal plants for thousands of years, with traces of plant-based medicine found in the earliest human civilizations. For thousands of years, peoples have used plants as medicine. In the initial stages, these medications were crude substance found in teas, tinctures, powers, poultices and other herbal products[3]. Eventually, information about medicinal plants was documented in herbals. In recent years, the use of plants as medicines has involved the isolation of active chemicals, beginning with the isolation of morphine from opium in the early nineteenth century. Drugs discovery from medicinal plants led to the isolation of early medications such as cocaine, codeine, digitoxin and qunine, as well as morphine, some of which are still in use[4]. According to the report of WHO about 21,000 medicinal plants are used for a variety of medical purposes. Traditional herbalists use about 2500 plants to cure common illnesses,

which is one of the greatest ways to treat illnesses in Indian medicine[5]. India is home to about 100 plant genera that are used in traditional medicinal systems around the world. India is second in terms of exporting approximately 45,000 plants, with 7000 plant species categorized as medicinal plants. Approximately 40% of the medicines in use are either entirely or partly derived from plants[5][6]. Plants are rich sources of phytochemicals & are often free from side effects, and due to their better compatibility with the human body, herbal medicines are widely recognized as an alternative to synthetic medicines. Herbal pharmaceuticals, often known as plants drugs, are medicines that contain chemical components obtained from plant that work on the human body to prevent diseases and to maintain or restore health[7]. These plant products are utilized in their raw form, or chemical compounds are isolated from them in the laboratory, and novel medications are occasionally produced by combining multiple isolated compounds before being used. Traditional non-standardized procedures used to separate a large number of herbal drugs from natural sources[8]. This combined with varying plant growth locations, problems with different vernacular names and the lack of standard procedures for cultivation, harvesting and post-harvesting, frequently results in the addition of impurities lowering the quality and effectiveness of final medicinal products and in some cases, causing adverse drug reactions[9]. In recent decades, attention has been placed on the standards of herbal drugs in order to reduce adulteration and protect the quality of these herbal medicines. The term Herbal drugs refers to all medical preparations made from plants, plant parts or plant products, with a little or no chemical manipulation[10]. In a broader sense, herbal medicines include herbs, herbal materials (leaves, flowers, fruits, seeds, stems, woods, barks, roots, rhizomes or other plant parts and active ingredients), herbal preparations, and finished products that contain plants, plant parts or other materials of plant origin or combinations thereof as their main ingredients[11]. In the context of phytopharmaceuticals, the term "herbal drugs" refers to plants or parts of plants that are used to cure various disorders. It first collects Coll or harvests, then dries and stores it before isolating and using it. The use of herbal substances as medicine is the oldest kind of treatment known to delicacy, and it has been employed by all nations throughout history[12]. Ancient humans were fully aware of their dependency on nature for a decent healthy life, and since then, humankind has relied on a range of plant resources for food, housing, clothing, and medicine to cure an infinite number of maladies[13]. The first written documents documenting the use of plants in healing were found on Mesopotamian clay tablets and Egyptian papyrus. Led by nature, taste, and experience, prehistoric men and women treated illnesses with plant parts, animal parts, and minerals that were not commonly consumed[14]. Primeval people learnt by trial and error how to distinguish between useful plants with positive effects and those that

were inactive or dangerous, as well as which processing methods or mixes needed to achieve consistent and optimal outcomes[15]. Even in ancient cultures, ethnic, ancestral, or tribal people gathered information about medicinal plants and created what is known as herbal pharmacopeia. Since ancient times, herbal medicines have been utilized to cure a variety of ailments. Medicinal plants have had a significant impact in global health. Despite significant developments in modern medicine over the last few decades, plants continue to play an essential role in health care[16]. Natural products have been our most successful source of medicine. Each plant functions as a factory, capable of producing an infinite number of very complex and uncommon chemical molecules whose structures would otherwise remain unimaginable[17]. There are at least 120 separate chemical molecules produced from plants that are regarded major medications in use today in the world, while several other drugs are simple synthetic modifications of the natural products[18]. WHO has provided several terminology related to herbal medications based on their definitions. Herbal medications encompass herbs, herbal ingredients, herbal preparations, and completed herbal products. In some places, herbal remedies may include natural organic or inorganic active components that are not derived from plants[19]. Herbs are crude plant materials such as leaves, flowers, fruit, seeds, stalks, wood, bark, roots, rhizomes, and other plant components that might be whole, fragmented, or powdered. Herbal materials include, in addition to herbs, fresh juices, gums, fixed oils, essential oils, resins, and dry herb powders[20]. Herbal preparations serve as the foundation for completed herbal medicines and might comprise powdered herbal components as well as extracts, tinctures, and fatty oils. They are created through extraction, fractionation, purification, concentration, and other physical or biological processes[21]. Drug discovery from herbal phytotherapy is a multi-stage process. The discovery of potential medicinal plants using traditional knowledge and ethnobotanical research is the prime step in drug discovery from herbal phytotherapy[22]. The next step is the harvesting and processing of plants, extraction, and isolation of phytochemicals. Finally, recognition of compounds' biological activity, safety, and effectiveness through various testing methods. Lately, following the technological process's development and emergence of efficient and precise methods for phytochemical extraction and analysis, many new drugs and treatment methods have been discovered[23]. Nevertheless, the field continues to face such widespread issues as plant resources sustainability, products' standardization, and regulatory issues. However, the potential of herbal phyto-therapy in drug discovery remains immense. In botanical literature, "herb" refers specifically to non-woody vascular plants, including annuals, biennials, and some perennials, particularly monocots, lacking persistent woody stems[24]. However, in pharmacy, "herb" is used more

broadly as a synonym for "plant," encompassing herbs, shrubs, and trees. Medicine, derived from the Latin “Ars medicina” meaning the art of healing, encompasses both science and art aimed at restoring health by preventing and treating illness in humans[25]. While prehistoric traditional medicine often relied on ritualistic and mystical use of plants, animal parts, and minerals, contemporary medicine utilizes modern methodologies for diagnosis and treatment. Traditional forms of medicine such as Traditional Chinese Medicine (TCM), Ayurveda, and Unani have evolved into more organized systems, reflecting cultural and regional influences[26]. The diverse forms of herbal materials and preparations, outlining the various plant parts involved and the processes by which they are processed and combined to create finished herbal products. It emphasizes the range of methods used globally, such as steaming, roasting, or mixing with other substances like honey or alcohol. Herbal preparations can take the form of powders, extracts, tinctures, or fatty oils, which are derived through extraction and purification processes[27]. The final products, whether derived from a single herb or a mixture, may include additional excipients alongside the active herbal ingredients.

2. Material and methods

Several scientific literature search engines, including MDPI, Wiley Online, Springer, PubMed, ResearchGate, Google Scholar, SpringerLink, Taylor & Francis, ScienceDirect, Academia.edu, Web of Science, Bentham, Scopus, Thieme, and SciFinder, were used to find publications that contained information on plant-derived natural products that were used as a source for drug discovery and development. "Medicinal plant," "drug discovery," and "plant-derived natural products" were the terminology utilized in the study. The literature covered natural compounds generated from plants that are used as good starting points for the development of new drugs. These papers were accurately constructed, critically analyzed, and thoroughly appraised. The process of finding and developing therapies from natural compounds in plants is a complex and multifaceted one that involves a number of crucial phases, each of which is critical to turning the promise of botanical molecules into effective drugs.

3. Results

3.1. Artemisinin

Artemisinin is a highly effective antimalarial drug derived from the sweet wormwood plant, *Artemisia annua*. Its discovery in 1972 by Chinese scientist Tu Youyou marked a significant breakthrough in the

fight against malaria, earning her the Nobel Prize in Physiology or Medicine in 2015[28]. Artemisinin is particularly potent against Plasmodium falciparum, the parasite responsible for the most severe and deadly form of malaria. The drug operates by producing free radicals that damage the parasite's proteins, leading to its rapid death. This mechanism of action is unique and highly effective, especially when artemisinin is used in combination with other antimalarial drugs in what is known as Artemisinin-based Combination Therapy (ACT)[29]. ACTs are the gold standard for malaria treatment worldwide, as they not only enhance the efficacy of artemisinin but also help prevent the development of drug resistance. Beyond its primary use in malaria treatment, artemisinin has shown promise in other medical fields[30]. Research is ongoing into its potential applications in cancer therapy. Preliminary studies suggest that artemisinin and its derivatives may inhibit the growth of various cancer cells and induce apoptosis, or programmed cell death, in tumours. This potential anticancer effect is thought to be due to artemisinin's ability to generate reactive oxygen species that damage cancer cell membranes and DNA[31]. However, while these findings are promising, more extensive clinical trials are necessary to confirm the safety and efficacy of artemisinin in cancer treatment. In addition to its medical applications, artemisinin's discovery and development highlight the importance of traditional medicine and natural products in modern pharmacology[32]. The journey from ancient Chinese herbal remedies to a Nobel Prize-winning drug underscores the value of integrating traditional knowledge with contemporary scientific research[33]. Artemisinin remains a vital tool in the global effort to combat malaria and potentially other diseases in the future.

3.2. Aspirin

Aspirin, also known as acetylsalicylic acid (ASA), is a widely used nonsteroidal anti-inflammatory drug (NSAID) with a rich history and diverse applications. Discovered in the late 19th century, aspirin has become a cornerstone in both pain management and cardiovascular disease prevention[34]. It works by inhibiting the enzyme cyclooxygenase (COX), which is crucial in the production of prostaglandins—compounds that mediate inflammation, pain, and fever. This mechanism makes aspirin effective in treating a variety of conditions, including headaches, muscle aches, arthritis, and minor injuries. Additionally, aspirin's antithrombotic properties, which prevent blood clots, make it valuable in reducing the risk of heart attacks and strokes[35]. Low-dose aspirin therapy is often recommended for individuals at high risk of these cardiovascular events, under medical supervision. Despite its benefits, aspirin is not without risks[36]. Long-term use can lead to gastrointestinal issues such as ulcers and bleeding,

particularly in individuals with a history of gastrointestinal problems. Aspirin is also associated with Reye's syndrome, a rare but serious condition that can occur in children and teenagers recovering from viral infections, which is why it is generally not recommended for this age group[37]. Beyond its traditional uses, aspirin is being explored for its potential in cancer prevention and treatment. Some studies suggest that regular aspirin use may reduce the risk of certain cancers, such as colorectal cancer, by inhibiting tumour growth and metastasis[38]. However, these findings are still under investigation, and the long-term safety and efficacy of aspirin in cancer prevention require further study. Overall, aspirin's versatility and effectiveness make it a vital medication in modern medicine[39]. Its discovery and development underscore the importance of integrating traditional knowledge with contemporary scientific research, highlighting aspirin's enduring relevance in healthcare.

3.3. Atropine

Atropine is a tropane alkaloid and anticholinergic medication with a wide range of medical applications. It is derived from plants of the nightshade family, such as deadly nightshade (*Atropa belladonna*), Jimson weed, and mandrake[39]. First isolated in 1833, atropine has since become a crucial drug in modern medicine. It works by blocking the action of acetylcholine on muscarinic receptors, which are part of the parasympathetic nervous system[40]. This action makes atropine effective in treating bradycardia (abnormally slow heart rate), reducing salivation and bronchial secretions during surgery, and as an antidote for poisoning by organophosphates and certain types of mushrooms[41]. Atropine is also used in ophthalmology to dilate the pupils (mydriasis) and paralyze the accommodation reflex (cycloplegia) during eye examinations and treatments[42]. The drug's effects can last from several days to over a week, making it useful for therapeutic purposes but less so for routine eye exams[26]. Additionally, atropine is included in the World Health Organization's List of Essential Medicines, highlighting its importance in global health[43]. Despite its benefits, atropine can cause several side effects, including dry mouth, blurred vision, sensitivity to light, urinary retention, constipation, and an increased heart rate. It should be used with caution in individuals with conditions like closed-angle glaucoma, as it can exacerbate symptoms. While generally considered safe during pregnancy and breastfeeding, its use should be carefully monitored by a healthcare professional[44]. Atropine's versatility extends beyond its primary uses. Research is ongoing into its potential applications in treating other conditions, such as irritable bowel syndrome and certain types of nerve agent poisonings[45]. Its discovery and continued use underscore

the importance of natural compounds in the development of essential medications, bridging traditional herbal remedies and modern pharmacology.

3.4. Berberine

Berberine is a bioactive compound found in several plants, including barberry, goldenseal, Oregon grape, and tree turmeric. It has been used for thousands of years in traditional Chinese and Ayurvedic medicine to treat a variety of ailments[46]. Modern research has highlighted berberine's potential in managing several metabolic health conditions, such as diabetes, obesity, and heart disease. One of the primary mechanisms by which berberine works is by activating AMP-activated protein kinase (AMPK), an enzyme that plays a crucial role in regulating metabolism and energy balance within cells[47]. This activation helps improve insulin sensitivity, reduce blood sugar levels, and enhance lipid metabolism, making berberine a promising supplement for individuals with type 2 diabetes and high cholesterol. In addition to its metabolic benefits, berberine has demonstrated antimicrobial properties. Studies have shown that it can inhibit the growth of various bacteria, including *Staphylococcus aureus*, which is responsible for numerous infections[48]. Berberine's anti-inflammatory effects further contribute to its therapeutic potential, as chronic inflammation is a key factor in many diseases, including heart disease and diabetes. Moreover, berberine may support gut health by promoting a healthy balance of gut microbiota, which is essential for overall well-being[49]. Despite its numerous benefits, berberine is not without side effects. Common adverse effects include gastrointestinal issues such as diarrhoea, constipation, and stomach upset. It is also important to note that berberine can interact with certain medications, so individuals should consult with a healthcare provider before starting supplementation[50]. While berberine shows great promise, more extensive clinical trials are needed to fully understand its long-term safety and efficacy. Overall, berberine's multifaceted benefits make it a valuable natural compound with potential applications in managing metabolic disorders, infections, and inflammation[51]. Its long history of use in traditional medicine, combined with modern scientific research, underscores its significance in promoting health and wellness.

3.5. Caffeine

Caffeine, a naturally occurring stimulant found in coffee, tea, chocolate, and various energy drinks, is widely consumed globally for its ability to enhance alertness and reduce fatigue. Its primary mechanism involves blocking adenosine receptors in the brain, which are responsible for promoting sleep and

relaxation[52]. By inhibiting these receptors, caffeine temporarily increases the levels of other neurotransmitters, such as dopamine and norepinephrine, leading to heightened arousal and improved mood[53]. This stimulating effect can be beneficial for short-term cognitive performance, including improved concentration and reaction times. However, excessive consumption of caffeine can lead to negative side effects such as anxiety, insomnia, and increased heart rate. The tolerance to caffeine varies among individuals, with some people metabolizing it more quickly than others due to genetic differences[54]. Pregnant women and individuals with certain health conditions are often advised to limit their intake to avoid potential adverse effects. Despite these concerns, moderate caffeine consumption is generally considered safe for most people and can even offer health benefits, such as a reduced risk of certain diseases like Parkinson's and Alzheimer's[55]. The recommended daily limit is usually around 400 milligrams, equivalent to about four cups of brewed coffee. Understanding the balance between its stimulating effects and potential risks is essential for maintaining overall health and well-being.

3.6. Campothecin

Campothecin is a naturally occurring alkaloid with significant therapeutic potential, primarily known for its role in cancer treatment. It was first isolated from the Chinese tree *Campotheca acuminata* and has since been recognized for its ability to inhibit DNA topoisomerase I, an enzyme crucial for DNA replication and transcription[2]. By binding to this enzyme, campothecin induces DNA damage and prevents cancer cells from dividing, thus exhibiting potent anti-cancer properties. Despite its efficacy, campothecin has limitations, including poor solubility and significant toxicity, which can lead to side effects such as gastrointestinal issues and bone marrow suppression[3]. To overcome these challenges, several campothecin derivatives have been developed, such as irinotecan and topotecan. These modified compounds have been incorporated into clinical treatments, particularly for cancers such as colorectal cancer (irinotecan) and ovarian cancer (topotecan). Research continues to focus on improving the efficacy and reducing the toxicity of campothecin and its derivatives, with ongoing studies exploring their use in combination therapies and as part of personalized cancer treatment regimens[7]. The compound's unique mechanism of action and its impact on cancer cell proliferation make it a crucial area of interest in the development of novel anticancer strategies.

3.7. Cocaine

Cocaine is a powerful stimulant drug derived from the leaves of the coca plant, *Erythroxylum coca*, native to South America. As a central nervous system stimulant, it affects the brain by inhibiting the reuptake of neurotransmitters like dopamine, norepinephrine, and serotonin[56]. This blockage leads to increased concentrations of these chemicals in the brain, resulting in heightened alertness, euphoria, and increased energy. Cocaine is often used recreationally for its intense euphoric effects, but it carries significant risks and potential for addiction[57]. The drug can be consumed in various forms, including powdered cocaine, which is typically snorted or dissolved in water and injected, and crack cocaine, which is processed into a smokable form. Despite its stimulating effects, cocaine use can lead to severe health problems, including cardiovascular issues such as heart attack and stroke, neurological damage, and psychological effects like paranoia and hallucinations[58]. Long-term use can also result in addiction, characterized by compulsive drug-seeking behaviour and significant impairment in daily functioning. In addition to its recreational use, cocaine has some medical applications, such as a local anaesthetic in certain medical procedures, particularly in ophthalmology and ear, nose, and throat surgery[59]. However, due to its high potential for abuse and severe health risks, its medical use is highly restricted and monitored. Efforts to combat cocaine abuse include various treatment and prevention programs aimed at reducing addiction and its associated harms.

3.8. Codeine

Codeine is an opioid medication used primarily for its analgesic (pain-relieving) and antitussive (cough-suppressing) effects. It is commonly prescribed to treat mild to moderate pain and to relieve coughing associated with various conditions, such as colds or respiratory infections. Codeine is derived from the opium poppy and is metabolized in the liver to morphine, which is responsible for its pain-relieving effects[60]. As a part of the opioid class, codeine works by binding to opioid receptors in the brain and spinal cord, altering the perception of pain and emotional response to it. It is often combined with other medications, such as acetaminophen or aspirin, in combination products for enhanced efficacy in pain management. Despite its benefits, codeine carries risks of dependence, addiction, and tolerance with prolonged use[61]. Side effects can include drowsiness, constipation, nausea, and, in some cases, more severe issues such as respiratory depression. Because of these risks, its use is closely monitored, especially in patients with a history of substance abuse or those taking other central nervous system depressants[62]. In recent years, there has been increasing concern about the misuse of codeine, leading

to tighter regulations and more cautious prescribing practices[63][64]. The drug's use is also carefully managed in children due to the risk of severe respiratory side effects, particularly with certain formulations.

3.9. Colchicine

Colchicine is a medication primarily used to treat and prevent gout attacks and to manage familial Mediterranean fever (FMF). It is derived from the autumn crocus plant (*Colchicum autumnale*) and works by inhibiting the migration of white blood cells to inflamed areas, thereby reducing inflammation and pain[65]. In gout, colchicine alleviates symptoms by interfering with the process that leads to the formation of uric acid crystals in the joints, which cause pain and swelling[66]. For FMF, colchicine helps to prevent recurrent episodes of fever and inflammation. The medication is usually taken orally and can be used in various forms, including tablets and oral solutions. While effective, colchicine can have side effects such as gastrointestinal issues (nausea, vomiting, diarrhoea), and in high doses, it may lead to more serious complications like muscle weakness or bone marrow suppression. Therefore, careful dosage and monitoring are essential to minimize risks[67]. Colchicine's use has declined somewhat in Favor of other medications with fewer side effects, but it remains an important option in the management of gout and FMF, particularly when other treatments are not suitable or effective[65].

3.10. Digitoxin

Digitoxin is a cardiac glycoside used in the treatment of heart failure and certain types of arrhythmias. It is derived from the foxglove plant (*Digitalis lanata*) and functions by increasing the force of heart contractions (positive inotropic effect) and regulating heart rhythm[68]. Digitoxin achieves this by inhibiting the sodium-potassium ATPase enzyme, leading to an increase in intracellular calcium levels, which enhances the contractility of the heart muscle. Unlike digoxin, another commonly used cardiac glycoside, digitoxin has a longer half-life and is more lipophilic, which means it stays in the body longer and can be more potent[69]. However, this also means that it has a higher risk of toxicity, which can manifest as nausea, vomiting, confusion, and visual disturbances, and in severe cases, can lead to life-threatening arrhythmias. Because of its narrow therapeutic index and the availability of other cardiac glycosides with more favourable safety profiles, digitoxin is less commonly used today[70]. Careful dosing and regular monitoring of blood levels are essential to prevent toxicity and ensure therapeutic efficacy. Despite its reduced use, digitoxin remains a historical and important part of cardiac therapy[71].

3.11. Digoxin

Digoxin is a cardiac glycoside used to treat heart failure and atrial fibrillation. Derived from the foxglove plant (*Digitalis lanata*), digoxin increases the strength of heart muscle contractions (positive inotropic effect) and slows the heart rate (negative chronotropic effect)[72]. It achieves this by inhibiting the sodium-potassium ATPase enzyme, leading to increased intracellular calcium, which enhances the heart's pumping efficiency. The drug is administered orally or intravenously, with dosage adjusted based on individual patient needs and blood levels to avoid toxicity[73]. Common side effects include nausea, vomiting, dizziness, and visual disturbances, such as yellow or blurred vision. Serious toxicity can lead to severe arrhythmias and other complications[74]. Digoxin requires careful monitoring due to its narrow therapeutic index—the range between effective and toxic doses is small. Its use has decreased somewhat in Favor of newer treatments with improved safety profiles, but it remains an important option for managing certain heart conditions[75].

3.12. Emetine

Emetine is an alkaloid derived from the ipecacuanha plant (*Cephaelis ipecacuanha*), traditionally used as an emetic (to induce vomiting) and as an expectorant. It is known for its ability to stimulate the vomiting center in the brain, making it effective in cases of poisoning or overdose where inducing vomiting can be beneficial[76]. In addition to its use as an emetic, emetine has been utilized in the treatment of amoebic dysentery, caused by the parasite Entamoeba histolytica. It works by inhibiting protein synthesis in the parasite, thereby eliminating the infection[77]. However, due to its toxicity and side effects, such as gastrointestinal irritation and potential for severe adverse effects including cardiac toxicity, its use has largely been supplanted by other, more effective and safer treatments for both parasitic infections and as an emetic[78]. Emetine is also a subject of research for its potential in cancer treatment, given its ability to inhibit cellular protein synthesis and induce cell death, although its clinical use for this purpose is not yet established.

3.13. Ephedrine

Ephedrine is a sympathomimetic drug that acts as a stimulant, primarily affecting the cardiovascular and respiratory systems. It is derived from the plant *Ephedra sinica* and is chemically related to adrenaline[79]. Ephedrine is used in medicine for its bronchodilator effects, making it useful in treating conditions like asthma and chronic obstructive pulmonary disease (COPD). It works by stimulating alpha and beta-

adrenergic receptors, leading to relaxation of bronchial smooth muscles and increased airflow[80]. Additionally, ephedrine has vasoconstrictive properties, which can raise blood pressure, making it valuable in managing hypotension during surgery or in certain cases of shock. It is also used as a nasal decongestant due to its ability to constrict blood vessels in the nasal passages[81]. Despite its benefits, ephedrine can cause side effects such as increased heart rate, hypertension, insomnia, and nervousness. Its use has been restricted in some countries due to concerns about potential abuse and severe adverse effects, especially in higher doses or when combined with other stimulants[80]. Ephedrine is also a precursor in the illicit manufacture of methamphetamine, leading to further regulatory controls on its distribution.

3.14. Ipecac

Ipecac is derived from the root of the *Cephaelis ipecacuanha* plant and has traditionally been used as an emetic to induce vomiting. Its active compounds, emetine and cephaeline, stimulate the vomiting centre in the brain and the gastrointestinal tract, leading to expulsion of stomach contents[77]. Historically, ipecac syrup was commonly used in cases of poisoning or overdose to help eliminate toxins from the stomach. However, its use has declined due to concerns about safety and effectiveness. Inducing vomiting is not always beneficial or safe in poisoning cases, and the American Academy of Paediatrics and other health organizations now generally recommend other interventions such as activated charcoal or specific antidotes[82]. Ipecac can also have adverse effects, including persistent nausea, diarrhoea, and in rare cases, more severe complications such as cardiac toxicity, especially with prolonged or excessive use[77]. Due to these concerns and the availability of more effective treatments, ipecac syrup is no longer widely recommended or used in modern medical practice.

3.15. Morphine

Morphine is a potent opioid analgesic derived from the opium poppy (*Papaver somniferum*). It is primarily used for the management of severe pain, such as that experienced after surgery, trauma, or in chronic pain conditions like cancer[83]. Morphine works by binding to opioid receptors in the brain and spinal cord, which alters the perception of pain and produces a sense of euphoria[84]. Morphine is administered in various forms, including oral tablets, injectable solutions, and extended-release formulations, depending on the clinical situation and the patient's needs. While effective for pain relief, it has a high potential for abuse and addiction due to its euphoric effects. Its use is associated with side effects such as

drowsiness, constipation, nausea, and respiratory depression[85]. Due to its narrow therapeutic index and the risk of dependence, morphine use is carefully managed, often involving dose adjustments and monitoring for signs of misuse or overdose[86]. In clinical practice, it is usually part of a broader pain management strategy, sometimes combined with other medications to optimize pain control while minimizing side effects and risks.

3.16. Nicotine

Nicotine is a potent chemical found in tobacco plants, known for its stimulating effects on the central nervous system. When consumed, it activates receptors in the brain, leading to increased alertness, improved mood, and temporary feelings of pleasure[87]. However, nicotine is also highly addictive, which makes it difficult for users to quit smoking or using other tobacco products. The addictive nature of nicotine is due to its ability to rapidly enhance dopamine levels in the brain, creating a reinforcing effect that encourages continued use[88]. This addiction contributes significantly to the broader health risks associated with smoking, including heart disease, lung cancer, and respiratory issues. Nicotine's impact is not limited to addiction. It can raise heart rate and blood pressure, potentially leading to cardiovascular problems. Despite these risks, nicotine is also used in various cessation aids like patches and gum, which help individuals quit smoking by providing controlled doses of nicotine to reduce withdrawal symptoms[89]. Overall, while nicotine itself is not the sole cause of tobacco-related diseases, its addictive properties and its role in encouraging continued tobacco use make it a significant concern for public health.

3.17. Papaverine

Papaverine is a vasodilator and smooth muscle relaxant derived from the opium poppy. It is primarily used in medicine to treat conditions involving smooth muscle spasms, such as in the treatment of erectile dysfunction and certain types of vasospasm. Papaverine works by relaxing the smooth muscles and dilating blood vessels, which improves blood flow[90]. It is sometimes used in combination with other medications to enhance its effects or target specific medical issues. Though it has therapeutic uses, papaverine is not commonly used today due to the availability of more effective or safer alternatives[91]. Its use is generally limited to specific clinical situations where other treatments are less suitable. Pilocarpine is a medication primarily used to treat dry mouth (xerostomia) and to manage intraocular pressure in conditions like glaucoma. It is a muscarinic agonist, which means it stimulates the

muscarinic receptors in the body, leading to increased secretion from salivary glands and improved moisture in the mouth[92]. In the treatment of glaucoma, pilocarpine helps reduce intraocular pressure by increasing the outflow of aqueous humour from the eye. In addition to its primary uses, pilocarpine may be employed in certain diagnostic tests to assess the function of sweat glands[90]. It can be administered topically as eye drops or systemically in oral form, depending on the condition being treated. While effective, pilocarpine can have side effects such as sweating, nausea, and gastrointestinal discomfort, reflecting its broad effects on various muscarinic receptors throughout the body.

3.18. Pilocarpine

Pilocarpine is a medication used primarily to treat conditions related to dry mouth and glaucoma. It is a muscarinic agonist, which means it stimulates muscarinic receptors in the body[93]. Pilocarpine is commonly prescribed to help increase saliva production in individuals with dry mouth, which can be caused by conditions such as Sjögren's syndrome or as a side effect of certain medications or cancer treatments[94]. It is used in the treatment of glaucoma, particularly in emergency situations where rapid reduction of intraocular pressure is needed. Pilocarpine works by causing the muscles around the eye to contract, which helps to open up the drainage channels in the eye and reduce pressure[95]. In both cases, pilocarpine works by mimicking the effects of acetylcholine, a neurotransmitter that activates various body functions. The most common side effects include sweating, nausea, and increased salivation, but its use is generally well-tolerated when prescribed appropriately[96].

3.19. Quinine

Quinine is a chemical compound derived from the bark of the cinchona tree, native to South America. Historically significant, it has been used for centuries as a treatment for malaria, a serious infectious disease caused by parasites transmitted through mosquito bites[97]. Quinine works by disrupting the ability of the malaria parasites to digest haemoglobin in red blood cells, thereby inhibiting their growth and reproduction. Its use as a malaria treatment dates back to the 17th century, when it was introduced to Europe from South America[98]. Despite its effectiveness, quinine can have significant side effects, including nausea, tinnitus, and in severe cases, cinchonism, which is a toxic reaction characterized by headache, visual disturbances, and other symptoms[99]. Due to these potential side effects, its use has largely been supplanted by more modern antimalarial drugs such as artemisinin-based combination therapies. Quinine also has a historical role in the development of tonic water, a popular beverage that

was originally used as a malaria prophylactic due to its quinine content[100]. While modern tonic water contains much lower concentrations of quinine compared to therapeutic doses, it retains a trace of the compound.

3.20. Reserpine

Reserpine is a drug derived from the Rauwolfia serpentina plant, traditionally used in Indian medicine. It acts primarily as an antihypertensive and antipsychotic medication. Reserpine works by depleting neurotransmitters such as norepinephrine, dopamine, and serotonin from nerve endings, which helps to lower blood pressure and alleviate symptoms of certain psychiatric conditions, such as schizophrenia and agitation[101]. Historically, reserpine was a significant treatment for high blood pressure and was used to manage mental health disorders before the advent of more modern medications[102]. Its effects are due to its action on the central nervous system, particularly by blocking the vesicular monoamine transporter (VMAT) that stores neurotransmitters in nerve endings[103]. Despite its effectiveness, reserpine can cause a range of side effects, including depression, drowsiness, and nasal congestion, which led to its reduced use in favor of newer drugs with fewer side effects[104]. However, it remains an important drug in the history of psychopharmacology and antihypertensive treatment.

3.21. Santonin

Santonin is a chemical compound derived from the wormwood plant (*Artemisia cina*), historically used as an anthelmintic agent to treat intestinal worm infections. It has a broad-spectrum activity against various types of parasitic worms, including roundworms and hookworms[105]. Santonin works by causing paralysis in the worms, which allows the body's natural processes to expel them. Its use as a medication dates back to the 19th century, and it was once a standard treatment for helminthiasis (worm infections)[106]. However, its use has declined due to the development of more effective and safer anti-parasitic drugs. Santonin can cause side effects such as nausea, vomiting, and visual disturbances[107]. Its administration also requires careful dosing because of its potential toxicity and the risk of side effects. While it is no longer commonly used in modern medicine, santonin played a significant role in the history of parasitic disease treatment.

3.22. Scopolamine

Scopolamine is a tropane alkaloid derived from plants such as Scopolia and Datura. It has various medical uses due to its anticholinergic properties, which involve blocking the action of acetylcholine, a neurotransmitter involved in muscle contraction and various autonomic functions[108]. Medically, scopolamine is primarily used to prevent nausea and motion sickness, often administered as a transdermal patch that releases the drug slowly over time. It can also be used to treat muscle spasms and to dilate the pupils during ophthalmic exams[109]. In addition to its therapeutic uses, scopolamine has a history of use as a sedative and in pre-anaesthetic medications. However, it can cause side effects such as dry mouth, blurred vision, dizziness, and drowsiness[110]. Overdose or misuse can lead to more severe effects, including hallucinations and delirium. Due to its potent effects and potential for abuse, scopolamine is used under careful medical supervision, with its use carefully managed to balance its therapeutic benefits against potential risks[111].

3.23. Stevioside

Stevioside is a natural sweetener derived from the leaves of the *Stevia rebaudiana* plant. It is a type of steviol glycoside and is known for being much sweeter than sucrose (table sugar) while contributing virtually no calories[112]. Stevioside is used as a sugar substitute in various food and beverage products. The compound works by interacting with sweet taste receptors on the tongue, providing a sweet taste without affecting blood sugar levels, making it a popular choice for people with diabetes or those looking to reduce calorie intake[113]. Stevioside has been studied for its potential health benefits, including blood sugar regulation and blood pressure reduction, although more research is needed to fully understand these effects[114]. It is considered safe for consumption and is approved by various health authorities, including the U.S. Food and Drug Administration (FDA) and the European Food Safety Authority (EFSA), though the approval pertains mainly to highly purified extracts rather than whole stevia leaves[115].

3.24. Strychnine

Strychnine is a potent and highly toxic alkaloid derived from the seeds of the *Strychnos nux-vomica* tree. It is a powerful neurotoxin that works by blocking inhibitory neurotransmission in the central nervous system, particularly by inhibiting the action of glycine, a neurotransmitter that helps regulate muscle relaxation[116]. Due to its action, strychnine causes severe muscle spasms and convulsions, and in high

doses, it can lead to respiratory failure and death. Historically, it has been used as a pesticide and in some traditional medicines, but its extreme toxicity limits its application[117]. In medical settings, strychnine is rarely used and is mostly studied for its toxicological effects. It is classified as a highly hazardous substance and is handled with extreme caution to prevent accidental poisoning. Its use is generally limited to research purposes due to the high risk associated with exposure.

3.25. Taxol

Taxol, also known as paclitaxel, is a chemotherapy drug used to treat various types of cancer, including ovarian, breast, lung, and pancreatic cancers[118]. It is derived from the bark of the Pacific yew tree (*Taxus brevifolia*), though synthetic production methods have been developed to increase supply. Taxol works by interfering with the normal function of microtubules during cell division[119]. It stabilizes microtubules and prevents their disassembly, which disrupts the mitotic spindle and halts the process of cell division, leading to cancer cell death. While effective, Taxol can cause side effects such as nausea, hair loss, peripheral neuropathy, and bone marrow suppression. Its use requires careful monitoring and management of side effects[120]. Taxol has significantly advanced cancer treatment, especially when combined with other chemotherapy agents.

3.26. Theobromine

Theobromine is a natural compound found in cocoa beans, tea leaves, and certain other plants. It is a methylxanthine, similar to caffeine, and has stimulant, diuretic, and vasodilatory effects[121]. In the body, theobromine acts as a mild stimulant by inhibiting phosphodiesterase, which increases cyclic AMP levels and promotes relaxation of smooth muscles, including those in the bronchi. This makes it useful for relieving cough and improving breathing[122]. It also has a mild diuretic effect, increasing urine production. While theobromine is generally considered safe in moderate amounts for most people, it can be toxic in high doses. It is particularly dangerous for pets, such as dogs and cats, who metabolize it more slowly and are susceptible to theobromine poisoning from chocolate ingestion[123]. Symptoms of theobromine toxicity include restlessness, rapid heart rate, and seizures. Theobromine contributes to the bitter taste of chocolate and is also studied for its potential health benefits, such as cardiovascular protection and improved cognitive function.

3.27. Theophylline

Theophylline is a medication used primarily for treating respiratory conditions such as asthma and chronic obstructive pulmonary disease (COPD). It belongs to a class of drugs known as xanthines, which also includes caffeine and theobromine. Theophylline works by relaxing the muscles around the airways, which helps to open them and improve airflow[123]. It achieves this by inhibiting the enzyme phosphodiesterase, leading to increased levels of cyclic AMP, which causes bronchodilation. Additionally, theophylline has anti-inflammatory effects that contribute to its therapeutic benefits[122]. The drug is typically administered orally in the form of tablets or capsules and is used in both acute and chronic management of respiratory conditions. However, theophylline has a narrow therapeutic window, meaning that the difference between an effective dose and a toxic dose is small[121]. Side effects can include nausea, vomiting, insomnia, and tremors, and in higher doses, more severe effects like arrhythmias or seizures may occur[123]. Due to these potential risks, theophylline therapy requires regular monitoring of blood levels to ensure safety and efficacy.

3.28. Thymol

Thymol is a natural compound with the chemical formula $C_{10}H_{14}O$, found predominantly in thyme oil, as well as in other essential oils like oregano and Savory. It is a type of monoterpene phenol[124]. Thymol is known for its antiseptic, antifungal, and antibacterial properties. It is commonly used in various medical and health applications, including as a preservative in foods, in mouthwashes, and in topical antiseptics. Its effectiveness against microorganisms makes it valuable in both medicinal and industrial contexts[125]. In addition to its antimicrobial properties, thymol is also used in traditional medicine for its potential anti-inflammatory and analgesic effects[126]. It has been studied for its ability to help treat respiratory conditions and other ailments due to its soothing and healing properties. While generally considered safe in appropriate amounts, excessive use of thymol can cause irritation or allergic reactions in some individuals[127]. It is important to use thymol-containing products according to recommended guidelines to avoid adverse effects.

3.29. Vinblastine

Vinblastine is a chemotherapy drug derived from the periwinkle plant (*Catharanthus roseus*). It is used in the treatment of various cancers, including Hodgkin's lymphoma, non-Hodgkin's lymphoma, testicular

cancer, and certain types of leukaemia[128]. Vinblastine works by inhibiting the process of cell division. It specifically disrupts the formation of microtubules, which are essential components of the mitotic spindle that separates chromosomes during cell division[129]. By preventing the proper formation of this spindle, vinblastine effectively halts cancer cell proliferation and induces cell death. Common side effects of vinblastine include nausea, vomiting, hair loss, constipation, and myelosuppression (which can lead to reduced blood cell counts and increased susceptibility to infections)[130]. Due to its potent effects and side effects, vinblastine is administered under careful medical supervision, often in combination with other chemotherapy agents to enhance efficacy and minimize resistance.

3.30. Vincristine

Vincristine is a chemotherapy drug derived from the periwinkle plant (*Catharanthus roseus*), similar to vinblastine. It is used to treat various cancers, including leukaemia (particularly acute lymphoblastic leukaemia), lymphomas, and some solid tumours such as neuroblastoma[131]. Vincristine works by disrupting cell division by binding to tubulin, a protein that forms microtubules. This interference prevents the proper formation of the mitotic spindle, which is crucial for chromosome separation during cell division[132]. As a result, vincristine halts the proliferation of cancer cells, leading to their death. Common side effects of vincristine include peripheral neuropathy (nerve damage), constipation, hair loss, and bone marrow suppression, which can lead to anaemia, infection, and bleeding issues[133]. Due to these potential side effects, vincristine is carefully dosed and monitored during treatment. It is often used in combination with other chemotherapy agents to maximize effectiveness and manage resistance[132].

Drugs	Common name	Scientific name	Pharmacological action	Reference
Artemisinin	Sweet wormwood	*Artemisia annua* L.	Antimalarial	[29]
Aspirin	White willow	*Salix alba* L.	Reduces pain & inflammation	[134]
Atropine	Belladonna	*Atropa belladonna* L.	Anticholinergic	[135]
Berberine	Barberry	*Berberis vulgaris* L.	Antidiabetic, hepatoprotective	[47]
Caffeine	Coffee	*Coffea arabica* L.	CNS stimulant	[54]
Camptothecin	Happy tree	*Camptotheca acuminata* Dence.	Treatment of ovarian and small cell lung cancer	[129]
Cocaine	Coca plant	*Erythroxylum coca* Lam.	Anaesthetic	[136]
Codeine	Poppy	*Papaver somniferum* L.	Pain reliever, suppresses coughing	[137]
Colchicine	Autumn crocus	*Colchicum autumnale* L.	Antigout, Anti-inflammatory	[65]
Digitoxin	Foxglove	*Digitalis purpurea* L.	Cardiotonic	[71]
Digoxin	Woolly foxglove	*Digtalis lanata* Ehrh	Cardiotonic	[74]
Emetine	Ipecacuanha	*Carapichea ipecacuanha* (Brot.)L. Andersson	Emetic, Amebicide	[77]
Ephedrine	Chinese ephedra	*Ephedra sinica* Stapf	Asthma, Treating common cold	[79]
Ipecac	Ipecacuanha	*Carapichea ipecacuanha* (Brot.) L. Andersso	Induce vomiting	[82]
Morphine	Poppy	*Papaver somniferum* L	Analgesic & sedative properties	[84]
Nicotine	Tobacco	*Nicotiana tabacum* L.	Analgesic	[88]
Papaverine	Poppy	*Papaver somniferum* L.	Smooth muscle relaxant	[90]
Pilocarpine	Jaborandi	*Pilocarpus microphyllus* Stapf ex Wardlew	Reduces pressure in eye	[95]
Quinine	Quina	*Cinchona officinalis* L.	Antimalarial	[100]
Reserpine	Patalagarar	*Rauwolfia serpentina* (L.)Benth. ex Kurz	Blood pressure	[103]

Drugs	Common name	Scientific name	Pharmacological action	Reference
Santonin	Drooping Sea-wormwood	*Artemisia maritima* L.	Ascaricide	[106]
Scopolamine	Henbane	*Hyoscyamus niger* L.	Eases motion sickness	[138]
Stevioside	Sugar leaf	*Stevia rebaudiana* (Bertoni) Bertoni	Sweetener	[112]
Strychnine	Nox-vomica	*Strychnos nux-vomica* L.	CNS stimulant	[117]
Taxol	Pacific yew	*Taxus brevifolia* Nutt	Antitumor	[118]
Theobromine	Cocoa tree	*Theobroma cacao* L.	Diuretic, vasodilator	[123]
Theophylline	Tea	*Camellia sinensis* (L) Kuntze.	Asthma & Chronic obstructive pulmonary disease	[124]
Thymol	Thyme	*Thymus vulgaris* L.	Antiseptic	[139]
Vinblastine	Sadabahar	*Cantharanthus roseus* (L.) G Don	Combats hodgkins disease	[128]
Vincristine	Sadabahar	*Cantharanthus roseus* (L.) G Don	Anticancer	[133]

Table 1. Herb and their pharmacological actions against disease.

4. Discussion

Aromatherapy has been used for thousands of years. Ancient cultures in China, India, Egypt, and elsewhere incorporated aromatic plant components in resins, balms, and oils. y. Aromatherapy uses aromatic essential oils medicinally to improve the health of the body, mind, and spirit[19]. It enhances both physical and emotional health. Researchers study traditional medicine practices to identify plants used for specific ailments[140]. This involves working with indigenous knowledge and practitioners to gather information about plant usage. Plants identified through ethnobotanical research are analyzed for their chemical constituents[6]. This involves isolating and identifying the compounds that may have therapeutic effects. The isolated compounds are tested in vitro (in the lab) and in vivo (in animal models)

to evaluate their efficacy and safety[17]. This helps determine whether the compounds have potential as new drugs. Promising compounds undergo clinical trials to assess their effectiveness and safety in humans. This process involves several phases and can take years. If clinical trials are successful, the drug must be approved by regulatory agencies before it can be marketed and prescribed.

5. Conclusion

Exploring traditional phytotherapy can lead to the discovery of new and effective treatments that might not be found through synthetic drug development alone. It highlights the value of traditional knowledge and the potential for integrating it with modern scientific techniques to advance medical treatments[27]. For many years, plants have been recognized as a vital source of therapeutic agents by the pharmaceutical and biotechnology industry. A wide range of modern drugs are of plant origin. Drug development from medicinal plants is currently being studied using a multimodal strategy that combines molecular, phytochemical, biological, and botanical techniques [49]. New and significant leads against a variety of pharmacological targets, such as HIV/AIDS, cancer, malaria, Alzheimer's, and pain, are still being discovered through medicinal plant drug discovery [138]. A number of plant-based natural product medications, such as arteether, galantamine, nitisinone, and tiotropium, have either just hit the market or are presently undergoing late-stage clinical trials [55]. With the advance of biotechnologies, traditional medicines have been improved and medicinal plants are nowadays used as the main sources for the discovery of new pharmaceutical molecules[3]. This work aimed to describe in a time a general view on the concept of pharmacognosy and to put a particular emphasis on phytotherapy as an effective therapeutic means. This work is an essential prerequisite for the extension of phytotherapy.

Statements and Declarations

Author Contributions

Conceptualization, S.K.B. and A.K.B.; methodology, B.P. and A.K.B.; Original draft preparation, B.P. and A.K.B. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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References

1. ^*Kamsu-FoguemB, FoguemC (2014). "Adverse drug reactions in some african herbal medicine: Literature review and stakeholders' interview." Integrative Medicine Research. 3:126–132. doi:10.1016/j.imr.2014.05.001.*
2. a, b*EjiohuoO, FolamiS, MaigoroAY (2024). "Calendula in modern medicine: Advancements in wound healing and drug delivery applications." European Journal of Medicinal Chemistry Reports. 12:100199. doi:10.1016/j.ejmcr.2024.100199.*
3. a, b, c*NgubaneNP, MabandlaMV, De GamaBZ (2024). "Global perspectives on the traditional approaches used in the treatment of schizophrenia: A systematic review." Asian Journal of Psychiatry. 97:104081. doi:10.1016/j.ajp.2024.104081.*
4. ^*SartoriSB, SingewaldN (2019). "Novel pharmacological targets in drug development for the treatment of anxiety and anxiety-related disorders." Pharmacology and Therapeutics. 204:107402. doi:10.1016/j.pharmthera.2019.107402.*
5. a, b*JakimiukK, TomczykM (2024). "A review of the traditional uses, phytochemistry, pharmacology, and clinical evidence for the use of the genus alchemilla (rosaceae)." Journal of Ethnopharmacology. 320. doi:10.1016/j.jep.2023.117439.*
6. a, b*KhanamA, SinghG, NarwalS (2024). "Treatment and prevention of recurrent urolithiasis: Insights on molecular mechanism of occurrence and medical care." Food Chemistry Advances. 5:100751. doi:10.1016/j.focha.2024.100751.*
7. a, b*HouA, YangL, LüJ, YangL, KuangH, JiangH (2022). "A bibliometrics visualization analysis and hotspots prediction for natural product on osteoporosis research from 2000 to 2021." Journal of Future Foods. 2:326–337. doi:10.1016/j.jfutfo.2022.08.004.*

8. ^ChakrabortyD, GuptaK, BiswasS (2021). "A mechanistic insight of phytoestrogens used for rheumatoid art hritis: An evidence-based review." Biomedicine and Pharmacotherapy. 133. doi:10.1016/j.biopha.2020.111039.
9. ^AntonioAS, WiedemannLSM, GalanteEBF, GuimarãesAC, MatharuAS, Veiga-JuniorVF (2021). "Efficacy and sustainability of natural products in covid-19 treatment development: Opportunities and challenges in usin g agro-industrial waste from citrus and apple." Heliyon. 7. doi:10.1016/j.heliyon.2021.e07816.
10. ^WangW, IgeOO, DingY, HeM, LongP, WangS, WenX (2023). "Insights into the potential benefits of triphala p olyphenols toward the promotion of resilience against stress-induced depression and cognitive impairmen t." Current Research in Food Science. 6:100527. doi:10.1016/j.crfs.2023.100527.
11. ^MaruthiyodanS, MumbrekarKD, GuruprasadKP (2024). "Involvement of mitochondria in alzheimer's dise ase pathogenesis and their potential as targets for phytotherapeutics." Mitochondrion. 101868. https://doi.or g/10.1016/j.mito.2024.101868.
12. ^MaigaY, SanghoO, KonipoF, DialloS, CoulibalySDP, SangareM, PéréonY, GiumelliB, SanouM, CoulibalyA, Di alloS, DaouM, TraoréZ, AlbakayeM, TraoréHA, GuintoCO, OuologemM, Kuate-TegueuC, BouhassiraD, Cowa nR, NizardJ (2021). "Neuropathic pain in mali: The current situation, comprehensive hypothesis, which ther apeutic strategy for africa?" eNeurologicalSci. 22:100312. https://doi.org/10.1016/j.ensci.2021.100312.
13. ^BakrimS, HachlafiNE, KhalidA, AbdallaAN, OmariNE, AboulaghrasS, SakranAM, GohKW, MingLC, RaziP, BouyahyaA (2024). "Recent advances and molecular mechanisms of tgf-β signaling in colorectal cancer, wi th focus on bioactive compounds targeting." Biomedicine & Pharmacotherapy. 177:116886. https://doi.org/1 0.1016/j.biopha.2024.116886.
14. ^HeinrichM, AppendinoG, EfferthT, FürstR, IzzoAA, KayserO, PezzutoJM, ViljoenA (2019). "Best practice in re search – overcoming common challenges in phytopharmacological research." Journal of Ethnopharmacolo gy. 246:112230. https://doi.org/10.1016/j.jep.2019.112230.
15. ^OtvosRA, StillKBM, SomsenGW, SmitAB, KoolJ (2019). "Drug discovery on natural products: From ion chan nels to nachrs, from nature to libraries, from analytics to assays." SLAS DISCOVERY. 24(3):362–385. https://d oi.org/10.1177/2472555218822098.
16. ^EsmeetaA, AdhikaryS, DharshnaaV, SwarnamughiP, MaqsummiyaZU, BanerjeeA, PathakS, DuttaroyAK (2 022). "Plant-derived bioactive compounds in colon cancer treatment: An updated review." Biomedicine & P harmacotherapy. 153:113384. https://doi.org/10.1016/j.biopha.2022.113384.
17. a, b NemboEN, HeschelerJ, NguemoF (2020). "Stem cells in natural product and medicinal plant drug discove ry—an overview of new screening approaches." Biomedicine & Pharmacotherapy. 131:110730. https://doi.or g/10.1016/j.biopha.2020.110730.

18. ^FadeyiOJ, AkwuNA, LekhooaM, HayeshiR, AremuAO (2024). "Utilisation of medicinal plants for their antifertility activities: A bibliometric analysis of research endeavours from 1968 to 2023." Phytomedicine Plus. 4(3):100580. https://doi.org/10.1016/j.phyplu.2024.100580.

19. a, bSinghN, GargM, PrajapatiP, SinghPK, ChopraR, KumariA, MittalA (2023). "Adaptogenic property of asparagus racemosus: Future trends and prospects." Heliyon. 9(4):e14932. https://doi.org/10.1016/j.heliyon.2023.e14932.

20. ^ChenX, WeiC, ZhaoJ, ZhouD, WangY, ZhangS, ZuoH, DongJ, ZhaoZ, HaoM, HeX, BianY (2024). "Carnosic acid: An effective phenolic diterpenoid for prevention and management of cancers via targeting multiple signaling pathways." Pharmacological Research. 206:107288. https://doi.org/10.1016/j.phrs.2024.107288.

21. ^ZouaouiZ, EnnouryA, NhhalaN, RoussiZ, KabachI, NhiriM (2024). "Juniperus oxycedrus l. phytochemistry and pharmacological properties: A review." Scientific African. e02361. https://doi.org/10.1016/j.sciaf.2024.e02361.

22. ^ShikovAN, PozharitskayaON, MakarovVG, WagnerH, VerpoorteR, HeinrichM (2014). "Medicinal plants of the russian pharmacopoeia; their history and applications." Journal of Ethnopharmacology. 154(3):481–536. https://doi.org/10.1016/j.jep.2014.04.007.

23. ^AhlidjaW, AmegayiborEF, AddaeL, AborEK, KorsahHM, Opoku-KwabiD, ArmahFA, HennehIT (2024). "Pharmacological and phytochemical properties of a promising african medicinal plant, sterculia setigera delile: A systematic review." Scientific African. e02142. https://doi.org/10.1016/j.sciaf.2024.e02142.

24. ^AhmedIA, MikailMA, ZamakshshariNH, MustafaMR, HashimNM, OthmanR (2022). "Trends and challenges in phytotherapy and phytocosmetics for skin aging." Saudi Journal of Biological Sciences. 29(8):103363. https://doi.org/10.1016/j.sjbs.2022.103363.

25. ^AruwaCE, SabiuS (2023). "Adipose tissue inflammation linked to obesity: A review of current understanding, therapies and relevance of phyto-therapeutics." Heliyon. 10(1):e23114. https://doi.org/10.1016/j.heliyon.2023.e23114.

26. ^TheodoridisS, DrakouEG, HicklerT, ThinesM, Nogues-BravoD (2023). "Evaluating natural medicinal resources and their exposure to global change." The Lancet Planetary Health. 7(2):e155–e163. https://doi.org/10.1016/s2542-5196(22)00317-5.

27. a, bMouraLFWG, Da Silva NetoJX, LopesTDP, BenjaminSR, BritoFCR, MagalhãesFEA, FloreanEOPT, De Oliveira Bezerra De SousaD, GuedesMIF (2018). "Ethnobotanic, phytochemical uses and ethnopharmacological profile of genus cnidoscolus spp. (euphorbiaceae): A comprehensive overview." Biomedicine & Pharmacotherapy. 109:1670–1679. https://doi.org/10.1016/j.biopha.2018.10.015.

28. ^YangD, NingJ, ZhangY, XuX, ZhangD, FanH, WangJ, LuG (2024). "In vitro assessment of the anti-adenoviral activity of artemisinin and its derivatives." Virus Research. 349:199448. https://doi.org/10.1016/j.virusres.2024.199448.

29. a, bDe Faveri FaveroF, BastingRT, De FreitasAS, Da Silva Dias RabeloL, NonatoFR, ZafredRTT, De Oliveira SousaIM, De Cássia Almeida QueirozN, NapimogaJTC, De CarvalhoJE, FoglioMA (2024). "Artemisinin and deoxyartemisinin isolated from artemisia annua l. promote distinct antinociceptive and anti-inflammatory effects in an animal model." Biomedicine & Pharmacotherapy. 178:117299. https://doi.org/10.1016/j.biopha.2024.117299.

30. ^XieK, LiZ, ZhangY, WuH, ZhangT, WangW (2024). "Artemisinin and its derivatives as promising therapies for autoimmune diseases." Heliyon. e27972. https://doi.org/10.1016/j.heliyon.2024.e27972.

31. ^WangY, YuanH, ShenD, LiuS, KongW, ZhengK, YangJ, GeL (2024). "Artemisinin attenuated ischemic stroke induced pyroptosis by inhibiting ROS/TXNIP/NLRP3/Caspase-1 signaling pathway." Biomedicine & Pharmacotherapy. 177:116894. doi:10.1016/j.biopha.2024.116894.

32. ^JamshidiB, EtminanA, MehrabiA, ShooshtariL, Pour-AboughadarehA (2024). "Comparison of phytochemical properties and expressional profiling of artemisinin synthesis-related genes in various Artemisia species." Heliyon. e26388. doi:10.1016/j.heliyon.2024.e26388.

33. ^GuoY, ChenY, WangD, LiuG, ChenY, PengC, CaoT, LiuY, HuX, XuX, KeY, HuangS, WangT, LvZ (2024). "Artemisinin and its derivatives modulate glucose homeostasis and gut microbiota remodeling in a nutritional context." The Journal of Nutritional Biochemistry. 131:109687. doi:10.1016/j.jnutbio.2024.109687.

34. ^LunKK, TangM, LewinA, HarrisIA (2024). "Aspirin as Venous Thromboembolism Prophylaxis in Arthroplasty Patients: An Analysis of Clinical Practice Guidelines Recommendations." The Journal of Arthroplasty. 39 (10):2405–2412.e1. doi:10.1016/j.arth.2024.05.050.

35. ^HernandezF, ChavezH, GoemansSL, KirakosyanY, LuevanoCD, CanfieldD, LaurentLC, JacobsM, WoelkersD, TarsaM, Gyamfi-BannermanC, FischKM (2024). "Aspirin resistance in pregnancy is associated with reduced interleukin-2 (IL-2) concentrations in maternal serum: Implications for aspirin prophylaxis for preeclampsia." Pregnancy Hypertension. 37:101131. doi:10.1016/j.preghy.2024.101131.

36. ^TsaiP-Y, LeeC-I, TamH-L, SuM-T (2024). "Aspirin alleviates fibronectin-induced preeclampsia phenotypes in a mouse model and reverses fibronectin-mediated trophoblast invasiveness under hypoxia by regulating ciliogenesis and Akt and MAPK signaling." Biochemical Pharmacology. 227:116423. doi:10.1016/j.bcp.2024.116423.

37. ^YuS, GuoL, GuoH (2024). "Aspirin-free P2Y12 inhibitor monotherapy immediately after percutaneous coronary intervention: A systematic review." Heliyon. 10(15):e35741. doi:10.1016/j.heliyon.2024.e35741.

38. ^NussEE, HoffmanMK, GoudarSS, KaviA, MetgudM, SomannavarM, OkitawutshuJ, LokangakaA, TshefuA, BausermanM, TemboAM, ChombaE, CarloWA, FigueroaL, KrebsNF, JessaniS, SaleemS, GoldenbergRL, Kurheek, DasP, HibberdPL, AchiengE, NyongesaP, EsamaiF, LiechtyEA, BucherS, GocoN, Hemingway-FodayJ, MooreJ, McClureEM, SilverRM, DermanRJ, PatelA (2024). "Corrigendum to The impact of risk factors on aspirin's efficacy for the prevention of preterm birth. American Journal of Obstetrics & Gynecology MFM. Volume 5, Issue 10, October 2023, 101095." American Journal of Obstetrics & Gynecology MFM. 6(4):101309. doi:10.1016/j.ajogmf.2024.101309.

39. a, bZengW, ChuTw, ChowEYk, HuM, FokBSp, ChanJCn, YanBPy, TomlinsonB (2024). "Genetic factors related to aspirin resistance using the Multiplate® device in Hong Kong Chinese patients with stable coronary heart disease." Heliyon. 10(14):e34552. doi:10.1016/j.heliyon.2024.e34552.

40. ^AzizMA, KuppusamyR, MazumderK, HuiA, MaulviF, StapletonF, WillcoxM (2024). "Absorption and attachment of atropine to etafilcon A contact lenses." Contact Lens and Anterior Eye. 47(5):102246. doi:10.1016/j.clae.2024.102246.

41. ^ChiaA, NgoC, ChoudryN, YamakawaY, TanD (2023). "Atropine Ophthalmic Solution to Reduce Myopia Progression in Pediatric Subjects: The Randomized, Double-Blind Multicenter Phase II APPLE Study." Asia-Pacific Journal of Ophthalmology. 12(4):370–376. doi:10.1097/apo.0000000000000609.

42. ^Fernández-PintorB, PaniaguaG, GañánJ, Morante-ZarceroS, GarcinuñoRM, FernándezP, SierraI (2024). "Determination of atropine and scopolamine in honey using a miniaturized polymer-based solid-phase extraction protocol prior to the analysis by HPLC-MS/MS." Polymer. 298:126904. doi:10.1016/j.polymer.2024.126904.

43. ^JahromyMH, QomiM, FazelipourS, SamiN, FaaliF, KarimiM, MoghadamFA (2024). "Evaluation of curcumin-based ophthalmic nano-emulsion on atropine-induced dry eye in mice." Heliyon. 10(7):e29009. doi:10.1016/j.heliyon.2024.e29009.

44. ^YamJC, JonasJB, LamDSC (2023). "Low-Concentration Atropine Eye Drops for Myopia Progression." Asia-Pacific Journal of Ophthalmology. 12(4):345–346. doi:10.1097/apo.0000000000000617.

45. ^NilsenNG, GilsonSJ, PedersenHR, HagenLA, WildsoetCF, BaraasRC (2024). "The effect of topical 1 % atropine on ocular dimensions and diurnal rhythms of the human eye." Vision Research. 214:108341. doi:10.1016/j.visres.2023.108341.

46. ^LiuQ, TangY, JiangS, YuX, ZhuH, XieX, NingX (2024). "Mechanisms of action of berberine hydrochloride in planktonic cells and biofilms of Pseudomonas aeruginosa." Microbial Pathogenesis. 193:106774. doi:10.1016/j.micpath.2024.106774.

47. a, bQiaoW, NiuL, JiangW, LuL, LiuJ (2024). "Berberine ameliorates endothelial progenitor cell function and wound healing in vitro and in vivo via the miR-21-3p/RRAGB axis for venous leg ulcers." Regenerative Therapy. 26:458–468. doi:10.1016/j.reth.2024.06.011.

48. ^ParseghianL, KahrarianN, ArabanianAS, AlvandZM, MassudiR, RahimiM, RafatiH (2024). "Berberine-loaded nanoemulsions as a natural food preservative; the impact of femtosecond laser irradiation on the antibacterial activity." Heliyon. 10(17):e37283. doi:10.1016/j.heliyon.2024.e37283.

49. a, bMehraM, SheorainJ, BakshiJ, ThakurR, GrewalS, DhingraD, KumariS (2024). "Synthesis and evaluation of Berberine loaded Chitosan Nanocarrier for enhanced in-vitro antioxidant and anti-inflammatory potential." Carbohydrate Polymer Technologies and Applications. 7:100474. doi:10.1016/j.carpta.2024.100474.

50. ^ChenX, MeiX-Y, RenZ-M, ChenS-S, TongY-L, ZhangC-P, ChenJ, DaiG-H (2024). "Comprehensive insights into berberine's hypoglycemic mechanisms: A focus on ileocecal microbiome in db/db mice." Heliyon. 10(13):e33704. doi:10.1016/j.heliyon.2024.e33704.

51. ^MengJ, WangW, DingJ, GuB, ZhouF, WuD, FuX, QiaoM, LiuJ (2024). "The synergy effect of matrine and berberine hydrochloride on treating colibacillosis caused by an avian highly pathogenic multidrug-resistant Escherichia coli." Poultry Science. 103(10):104151. doi:10.1016/j.psj.2024.104151.

52. ^LukmanK, IbrahimS, MuhammadA, BabandiA, YakasaiHM, MuhammadJB, JagabaAH (2024). "Bacillus sp. KS38 strain for sustainable caffeine degradation: Isolation, identification and optimization using response surface methodology." Desalination and Water Treatment. 320:100628. doi:10.1016/j.dwt.2024.100628.

53. ^TeshomeT, GureA, KitteSA, TesfayeB, GonfaG (2024). "Electrochemical determination of caffeine in coffee and non-alcoholic drinks using g-C3N4-ZnO modified glassy carbon electrode." International Journal of Electrochemical Science. 19(9):100698. doi:10.1016/j.ijoes.2024.100698.

54. a, bBilondiHT, ValipourH, KhoshroS, JamilianP, OstadrahimiA, ZarezadehM (2024). "The effect of caffeine supplementation on muscular strength and endurance: A meta-analysis of meta-analyses." Heliyon. 10(15):e35025. doi:10.1016/j.heliyon.2024.e35025.

55. a, bKrugerTB, DixonMJ, OakmanJM, SmilekD (2024). "Examining the effects of caffeine during an auditory attention task." Consciousness and Cognition. 124:103729. doi:10.1016/j.concog.2024.103729.

56. ^Ávila-GámizF, Pérez-CanoAM, Pérez-BerlangaJM, Zambrana-InfantesEN, Mañas-PadillaMC, Gil-RodríguezS, TronelS, SantínLJ, De Guevara-MirandaDL (2024). "Sequential physical and cognitive training disrupts c

ocaine-context associations via multi-level stimulation of adult hippocampal neurogenesis." Progress in Neuro-Psychopharmacology and Biological Psychiatry. 111148. doi:10.1016/j.pnpbp.2024.111148.

57. ^*Romero-NoreñaA, Contreras-MartinezHJ, Mendivil-PerezM (2024). "Toxicology of anhydroecgonine methyl ester: A systematic review of a cocaine pyrolysis product." Toxicology Reports. 13:101690. doi:10.1016/j.toxrep.2024.101690.*

58. ^*ThibeaultKC, LeonardMZ, KondevV, EmersonSD, BethiR, LopezAJ, SensJP, NabitBP, ElamHB, WinderDG, PatelS, KiralyDD, GrueterBA, CalipariES (2024). "A Cocaine-Activated Ensemble Exerts Increased Control Over Behavior While Decreasing in Size." Biological Psychiatry. doi:10.1016/j.biopsych.2024.06.008.*

59. ^*MankameS, WorobeySJ, SackoTJ, PierceRC, Swinford-JacksonSE (2024). "Differential effects of deep brain stimulation on reinstatement of cocaine seeking in male and female rats." Neuroscience Letters. 836:137888. doi:10.1016/j.neulet.2024.137888.*

60. ^*ChenM, YuH (2023). "Efficacy of compound pholcodine syrup and compound codeine phosphate oral solution on lung cancer cough." Clinical Nutrition ESPEN. 58:495. doi:10.1016/j.clnesp.2023.09.209.*

61. ^*AjayiAF, AkhigbeRE (2021). "Apoptotic inducement of neuronal cells by codeine: possible role of disrupted redox state and caspase 3 signaling." Heliyon. 7(7):e07481. doi:10.1016/j.heliyon.2021.e07481.*

62. ^*VyhmeisterK, SierraCM (2022). "Codeine prescribing practices before and after the 2017 FDA warning at an academic health system." Journal of the American Pharmacists Association. 63(4):S20–S24. doi:10.1016/j.japh.2022.12.009.*

63. ^*McCoyJ, NielsenS, BrunoR (2023). "Development and validation of a brief screening tool for over-the-counter codeine dependence." Research in Social and Administrative Pharmacy. doi:10.1016/j.sapharm.2023.11.002.*

64. ^*BinjawharDN, MohammedsaeedW (2024). "pH-switchable hydrophobic deep eutectic solvent-based liquid phase microextraction for detecting morphine and codeine in whole blood samples followed by HPLC-UV." Journal of King Saud University - Science. 36(8):103303. doi:10.1016/j.jksus.2024.103303.*

65. ^a, ^b, ^c*LiuY-C, ZhouZ-K, YuM-M, WangL-J, ShouS-T, ChaiY-F (2024). "Colchicine poisoning: Case report of three homicides in a family." Heliyon. 10(11):e32407. doi:10.1016/j.heliyon.2024.e32407.*

66. ^*ChengZ, WongZY, RamkanthS, HeeCW, TsMS, KayarohanamS, BegumMY, KhannaK, KumarA, JanakiramanAK (2024). "Colchicine-capped ZnO nanoparticles: Elucidation of their cytotoxicity potential against MDA-MB 231 cancer cells." OpenNano. 18:100210. doi:10.1016/j.onano.2024.100210.*

67. ^*KirovH, CaldonazoT, RunkelA, MedinD, FischerJ, DallanLR, MukharyamovM, MejiaOA, JateneFB, DoenstT (2024). "Colchicine in Patients with Coronary Disease Undergoing Coronary Artery Bypass Surgery – A Met*

a-Analysis of Randomized Controlled Trials." The American Journal of Cardiology. 231:48–54. doi:10.1016/j.amjcard.2024.09.003.

68. ^ *BoscaroC, SchimdtG, CignarellaA, MasoL, BolegoC, TrevisiL (2024). "The antiangiogenic effect of digitoxin is dependent on a ROS-elicited RhoA/ROCK pathway activation." Biochemical Pharmacology. 222:116049. doi:10.1016/j.bcp.2024.116049.*

69. ^ *Sheikhi-KouhsarM, BagheriH, AlsaikhanF, AldhalmiAK, AhmedHH (2024). "Solubility of digitoxin in super critical CO2: Experimental study and modeling." European Journal of Pharmaceutical Sciences. 195:106731. doi:10.1016/j.ejps.2024.106731.*

70. ^ *IraciF, HerdegC, HolzwarthM, StorzMA (2023). "Of mixed vegetables and cardiac arrhythmias - Digitalis purpurea confused with Borago officinalis: A case series of accidental digitoxin intoxications." Journal of Cardiology Cases. 28(2):86–90. doi:10.1016/j.jccase.2023.04.007.*

71. a, b *JiangX, XuX, SongS, KuangH, LiuL, XuL, XuC (2022). "Colloidal gold-based immunochromatographic strip for the detection of digitoxin in human plasma." Chinese journal of analytical chemistry. 51(2):100220. doi:10.1016/j.cjac.2022.100220.*

72. ^ *ErkkiläO, HernesniemiJ, TynkkynenJ (2023). "The Association Between Digoxin Use and Long-Term Mortality After Acute Coronary Syndrome." The American Journal of Cardiology. 204:377–382. doi:10.1016/j.amjcard.2023.06.125.*

73. ^ *SeeC, WheelockKM, CaraballoC, KheraR, AnnapureddyA, MahajanS, LuY, KrumholzHM, MurugiahK (2023). "Patterns of Digoxin Prescribing for Medicare Beneficiaries in the United States 2013-2019." American Journal of Medicine Open. 10:100048. doi:10.1016/j.ajmo.2023.100048.*

74. a, b *SupervíaA, Caballero-BermejoAF, PuiguriguerJ, CórdobaF, Martínez-BaladrónA, CalladoF, Lobo-AntuñaV, FuentesE, Molina-SamperV, VertS, Ruíz-RuízF, Guijarro-EguinoaFJ, Martín-PérezB, OlmosS, Ruiz-AntoránB, Maza-VeraMT, PallàsO, ClimentB, Igartua-AstibiaM, GutiérrezE, NoguéS, Ferrer-DufolA, Burillo-PutzeG (2024). "Seven- and thirty-day mortality in digoxin poisoning: Results from the DIGITOX study." The American Journal of Emergency Medicine. 81:92–98. doi:10.1016/j.ajem.2024.04.048.*

75. ^ *HashimotoJ, FujitaE, TanimotoK, KondoS, Matsumoto-MiyaiK (2024). "Effects of cardiac glycoside digoxin on dendritic spines and motor learning performance in mice." Neuroscience. 541:77–90. doi:10.1016/j.neuroscience.2024.01.018.*

76. ^ *EilerDR, WimberlyBT, BilodeauDY, TaliaferroJM, ReiganP, RisslandOS, KieftJS (2024). "The Giardia lamblia ribosome structure reveals divergence in several biological pathways and the mode of emetine function." Structure. doi:10.1016/j.str.2023.12.015.*

77. ^ a, b, c, d SidorenkoVS, CohenI, DorjeeK, MinettiCA, RemetaDP, GaoJ, PotapovaI, WangHZ, HearingJ, YenW-Y, Ki mHK, HashimotoK, MoriyaM, DickmanKG, YinX, Garcia-DiazM, ChennamshettiR, BonalaR, JohnsonF, Wald eckAL, GuptaR, LiC, BreslauerKJ, GrollmanAP, RosenquistTA (2024). "Mechanisms of antiviral action and to xicities of ipecac alkaloids: Emetine and dehydroemetine exhibit anti-coronaviral activities at non-cardioto xic concentrations." Virus Research. 341:199322. doi:10.1016/j.virusres.2024.199322.

78. ^ DindaB, DindaS, DindaM, SarmaIS, MajumdarS, SahaS (2024). "Therapeutic potential of natural alkaloid emetine against emerging COVID-19 and future viral pandemics." European Journal of Medicinal Chemistr y Reports. 12:100173. doi:10.1016/j.ejmcr.2024.100173.

79. ^ a, b SchmidtS, ZeheM, HolzgrabeU (2022). "Characterization of binding properties of ephedrine derivatives t o human alpha-1-acid glycoprotein." European Journal of Pharmaceutical Sciences. 181:106333. doi:10.1016/j. ejps.2022.106333.

80. ^ a, b MayerA, MiskellyG (2023). "Chemical decontamination of methamphetamine and ephedrine using hous ehold hypochlorite bleach." Forensic Chemistry. 36:100538. doi:10.1016/j.forc.2023.100538.

81. ^ De La SernaR, Jurado-SánchezJ, Márquez-ÁlvarezC, Pérez-ParienteJ, Gómez-HortigüelaLA (2024). "A chira l zeolite material with improved enantioselective catalytic properties prepared from readily accessible ephe drine alkaloids." Microporous and Mesoporous Materials. 113083. doi:10.1016/j.micromeso.2024.113083.

82. ^ a, b FalangaCM, SteinbornC, MuratspahićE, Zimmermann-KlemdAM, WinkerM, KrennL, HuberR, GruberCW, GründemannCI (2022). "Ipecac root extracts and isolated circular peptides differentially suppress inflamma tory immune response characterised by proliferation, activation and degranulation capacity of human lym phocytes in vitro." Biomedicine & Pharmacotherapy. 152:113120. doi:10.1016/j.biopha.2022.113120.

83. ^ HanksGW, De ConnoF, ChernyN, HannaM, KalsoE, McQuayHJ, MercadanteS, MeynadierJ, PoulainP, Ripam ontiC, RadbruchL, CasasJRI, SaweJ, TwycrossRG, VentafriddaV (2001). "Morphine and alternative opioids in cancer pain: the EAPC recommendations." British Journal of Cancer. 84(5):587–593. doi:10.1054/bjoc.2001.1 680.

84. ^ a, b PaulAK, GuevenN, DietisN (2021). "Profiling the Effects of Repetitive Morphine Administration on Motor Behavior in Rats." Molecules. 26(14):4355. doi:10.3390/molecules26144355.

85. ^ BarrattDT, KlepstadP, DaleO, KaasaS, SomogyiAA (2024). "Pharmacokinetic and neuroimmune pharmaco genetic impacts on slow-release morphine cancer pain control and adverse effects." The Pharmacogenomic s Journal. 24(3). doi:10.1038/s41397-024-00339-w.

86. ^ GuoK-K, DengC-Q, LuG-J, ZhaoG-L (2018). "Comparison of analgesic effect of oxycodone and morphine on patients with moderate and advanced cancer pain: a meta-analysis." BMC Anesthesiology. 18(1). doi:10.118

6/s12871-018-0583-8.

87. ^ *RandallCA, SunD, RandallPA (2024). "A novel alcohol+nicotine co-use self-administration procedure revea ls sex differences and differential alteration of mesocorticolimbic TLR- and cholinergic-related neuroimmu ne gene expression in rats." Alcohol. 121:115–131. doi:10.1016/j.alcohol.2024.08.003.*

88. a, b *PhanL, ZareiK, Chen-SankeyJ, HackerK, AjithA, JewettB, ChoiK (2024). "Exposure to nicotine pouch mark eting and nicotine pouch experimentation among U.S. adults who use commercial tobacco." Preventive Me dicine Reports. 46:102868. doi:10.1016/j.pmedr.2024.102868.*

89. ^ *MercincavageM, WackowskiOA, JohnsonAC, YoungWJ, TanASL, DelnevoCD, StrasserAA, VillantiAC (2024). "Associations of educational and marketing messages with beliefs about nicotine and reduced nicotine ciga rettes." Preventive Medicine. 185:108056. doi:10.1016/j.ypmed.2024.108056.*

90. a, b, c *SarachevaK, DimitrovaD, NikolovaS, GledachevaV, MilushevaM, PenchevaM (2023). "A comparative st udy of the effects of papaverine and a new isoquinoline precursor on rat memory functions and motor acti vity." Neuroscience Applied. 2:102689. doi:10.1016/j.nsa.2023.102689.*

91. ^ *KazemzadehD, AbdulrahmanNH, ShlashNG, GholipoorS, KhalafIH, SayyahA, BajgiranFA, AkbariF, Ghanb arnezhadS, AghajaniS, SalehzadehA (2024). "The cytotoxic effect of conjugated iron oxide nanoparticle by Papaverine on colon cancer cell line (HT29) and evaluation the expression of CASP8 and GAS6-AS1 genes." Results in Chemistry. 7:101323. doi:10.1016/j.rechem.2024.101323.*

92. ^ *AtshanDA, ZalzalaMH (2024). "Papaverine attenuates the progression of alpha naphthylisothiocyanate in duce cholestasis in rats." Current Research in Pharmacology and Drug Discovery. 6:100177. doi:10.1016/j.crph ar.2024.100177.*

93. ^ *YangHW, KhoAR, LeeSH, KangBS, ParkMK, LeeCJ, ParkSW, WooSY, KimDY, JungHH, ChoiBY, YangWI, Song HK, ChoiHC, ParkJK, SuhSW (2024). "A phosphodiesterase 4 (PDE4) inhibitor, amlexanox, reduces neuroinfl ammation and neuronal death after pilocarpine-induced seizure." Neurotherapeutics. 21(4):e00357. doi:10.1 016/j.neurot.2024.e00357.*

94. ^ *LiJ, ChengX, XueL, LiuH (2024). "Ameliorative influence of Baijin Pills on lithium-pilocarpine-induced epile psy in mice: role of oxidative stress, neurotransmitters and multidrug resistant transporters." Phytomedicin e Plus. 4(2):100555. doi:10.1016/j.phyplu.2024.100555.*

95. a, b *MianP, MaurerJM, TouwDJ, VosMJ, RottierBL (2023). "Pharmacy compounded pilocarpine: An adequate s olution to overcome shortage of pilogel® discs for sweat testing in patients with cystic fibrosis." Journal of Cystic Fibrosis. 23(1):126–131. doi:10.1016/j.jcf.2023.09.014.*

96. ^ChandÍa-CristiA, GutiérrezDA, DulceyAE, LaraM, VargasL, LinY-H, Jimenez-MuñozP, LarenasG, XuX, Wang A, OwensA, DextrasC, ChenY, PintoC, MarínT, Almarza-SalazarH, AcevedoK, CancinoGI, HuX, RojasP, Ferrer M, SouthallN, HendersonMJ, ZanlungoS, MaruganJJ, RÁ (2024). "Prophylactic treatment with the c-Abl inhi bitor, neurotinib, diminishes neuronal damage and the convulsive state in pilocarpine-induced mice." Cell R eports. 43(5):114144. doi:10.1016/j.celrep.2024.114144.

97. ^DushnaO, DubenskaL, MartonM, HatalaM, VojsM (2023). "Sensitive and selective voltammetric method fo r determination of quinoline alkaloid, quinine in soft drinks and urine by applying a boron-doped diamond electrode." Microchemical Journal. 191:108839. doi:10.1016/j.microc.2023.108839.

98. ^BeerLC, HargisBM, VuongCN (2021). "Research Note: Evaluation of quinine as a chemoprophylactic candid ate against histomoniasis in turkeys." Poultry Science. 100(11):101469. doi:10.1016/j.psj.2021.101469.

99. ^CaoM, VialA, MinderL, GuédinA, FribourgS, AzémaL, FeuillieC, MolinariM, Di PrimoC, BarthélémyP, Chain JL (2023). "Aptamer-based nanotrains and nanoflowers as quinine delivery systems." International Journal of Pharmaceutics X. 5:100172. doi:10.1016/j.ijpx.2023.100172.

100. a, bMbalaJ-GM, MaweteDT, MakieseAN, KwiraviwePL, PanguBK, NguimiEB, KanyangaRC, PietersL, Degott eG, FrederichM, MatondoA, Van PeltN, CaljonG, PirotteB, MavingaBM, Bambi-NyanguileS-M (2023). "Synth esis and pharmacological evaluation of fluoro/chloro-substituted acetyl and benzoyl esters of quinine as a ntimalarial agents." Results in Chemistry. 7:101284. doi:10.1016/j.rechem.2023.101284.

101. ^FerrariniEG, PaesRS, BaldassoGM, De AssisPM, GouvêMC, De CiccoP, RaposoNRB, CapassoR, MoreiraELG, DutraRC (2022). "Broad-spectrum cannabis oil ameliorates reserpine-induced fibromyalgia model in mic e." Biomedicine & Pharmacotherapy. 154:113552. doi:10.1016/j.biopha.2022.113552.

102. ^UtaD, TsuboshimaK, MizumuraK, NishijoH, TaguchiT (2024). "Amitriptyline and duloxetine attenuate acti vities of superficial dorsal horn neurons in a rat reserpine-induced fibromyalgia model." Journal of Pharma cological Sciences. 156(3):180–187. doi:10.1016/j.jphs.2024.08.006.

103. a, bTelegaLM, BertiR, BlazhenetsG, DomogallaL-C, SteinackerN, OmraneMA, MeyerPT, CoenenVA, EderA-C, DöbrössyMD (2024). "Reserpine-induced rat model for depression: Behavioral, physiological and PET-base d dopamine receptor availability validation." Progress in Neuro-Psychopharmacology and Biological Psych iatry. 133:111013. doi:10.1016/j.pnpbp.2024.111013.

104. ^IkedaN, KawasakiM, BabaK, NishimuraH, FujitaniT, SuzukiH, MatsuuraT, OhnishiH, ShimizuM, SanadaK, NishimuraK, YoshimuraM, MaruyamaT, Conway-CampbellBL, OnakaT, TeranishiH, HanadaR, UetaY, Sakai A (2023). "Chemogenetic Activation of Oxytocin Neurons Improves Pain in a Reserpine-induced Fibromyalg ia Rat Model." Neuroscience. 528:37–53. doi:10.1016/j.neuroscience.2023.07.028.

105. ^BlayG, CardonaL, GarcíaB, PedroJR (2000). "The Synthesis of Bioactive Sesquiterpenes from Santonin." In Studies in natural products chemistry; 53–129. doi:10.1016/s1572-5995(00)80044-7.

106. a, bFerreiraJRO, CavalcantiBC, Da CostaPM, De ArantesFFP, De AlvarengaES, MalthaCRA, De Almeida Barbo saLC, MilitãoGCG, PessoaC, FerreiraPMP (2013). "Induction of G2/M arrest, caspase activation and apoptosi s by α-santonin derivatives in HL-60 cells." Toxicology in Vitro. 27(5):1458–1466. doi:10.1016/j.tiv.2013.03.010.

107. ^KimSH, SongJH, ChoiBG, KimHJ, KimTS (2006). "Chemical Modification of Santonin into a Diacetoxy Acet al Form Confers the Ability to Induce Differentiation of Human Promyelocytic Leukemia Cells via the Down -regulation of NF-κB DNA Binding Activity." Journal of Biological Chemistry. 281(19):13117–13125. doi:10.107 4/jbc.m510944200.

108. ^OyeniranOH, OmotoshoO-PI, AdemolaII, IbraheemO, NwagweOR, OnodugoCA (2024). "Lemon (Citrus lim on) leaf alkaloid-rich extracts ameliorate cognitive and memory deficits in scopolamine-induced amnesic r ats." Pharmacological Research - Modern Chinese Medicine. 100395. doi:10.1016/j.prmcm.2024.100395.

109. ^BalasubramanianC, RamaswamyRS (2024). "Evaluation of nootropic and neuroprotective properties of Si ddha drug Poorana Chandrothaya Chenthuram (PCC) in scopolamine-induced amnesia in mice." Phytome dicine Plus. 4(3):100585. doi:10.1016/j.phyplu.2024.100585.

110. ^RyuMS, YueY, LiC, YangH-J, ZhangT, WuX, JeongDY, ParkS (2024). "Moderate capsaicin-containing kochuja ng alleviates memory impairment through the gut-brain axis in rats with scopolamine-induced amnesia." Biomedicine & Pharmacotherapy. 178:117091. doi:10.1016/j.biopha.2024.117091.

111. ^TadayonN, RamazaniA, RezazadehS, NohoojiMG, AngouraniHR (2024). "Isolation and investigation of an tibacterial activities and cytotoxicity of atropine and scopolamine." Results in Chemistry. 10:101732. doi:10.1 016/j.rechem.2024.101732.

112. a, bDaiZ, NieM, ChenY, SongJ, XuY, ZhangZ, ZhangG, YanS, ZhangX, LiD (2023). "Lutein-stevioside nanoparti cle attenuates H2O2-induced oxidative damage in ARPE Cells." Deleted Journal. 13(3):1628–1635. doi:10.2659 9/fshw.2022.9250138.

113. ^JiangJ, QiL, WeiQ, ShiF (2022). "Maternal stevioside supplementation improves intestinal immune functio n of chicken offspring potentially via modulating gut microbiota and down-regulating the promoter methy lation level of suppressor of cytokine signaling 1 (SOCS1)." Animal Nutrition. 10:329–346. doi:10.1016/j.aninu. 2022.06.002.

114. ^CaiT, YeH, JiangH, LinC, LouC, WangW, YanZ, XueX, PanX, LinJ (2023). "Stevioside targets the NF-κB and M APK pathways for inhibiting inflammation and apoptosis of chondrocytes and ameliorates osteoarthritis i n vivo." International Immunopharmacology. 115:109683. doi:10.1016/j.intimp.2023.109683.

115. ^DuttaA, HossainMd A, SomadderPD, MoliMA, AhmedK, RahmanMM, BuiFM (2024). "Exploring the therapeutic targets of stevioside in management of Type 2 Diabetes by network pharmacology and in-silico approach." Diabetes & Metabolic Syndrome Clinical Research & Reviews. 18(8):103111. doi:10.1016/j.dsx.2024.103111.

116. ^SaitoY, YamanoueK, SegawaY, ItamiK (2020). "Selective Transformation of Strychnine and 1,2-Disubstituted Benzenes by C–H Borylation." Chem. 6(4):985–993. doi:10.1016/j.chempr.2020.02.004.

117. a, bHanI (2024). "Strychnine: post-mortem effects." Pathology. 56:S11. doi:10.1016/j.pathol.2023.12.043.

118. a, bNowrouziB, Torres-MonteroP, KerkhovenEJ, MartínezJL, Rios-SolisL (2023). "Rewiring Saccharomyces cerevisiae metabolism for optimised Taxol® precursors production." Metabolic Engineering Communications. 18:e00229. doi:10.1016/j.mec.2023.e00229.

119. ^StadlerM, KolarikM (2024). "Taxol is NOT produced sustainably by endophytic fungi! – A case study for the damage that scientific papermills can cause for the scientific communities." Fungal Biology Reviews. 49:100367. doi:10.1016/j.fbr.2024.100367.

120. ^ChiuP-L, LinM-C, HsuS-T, HoT-Y, ChenY-H, ChenC-C, ChenY-S (2024). "Rosmarinic acid Ameliorates neuronal regeneration in the bridging silicone rubber conduits of the sciatic nerve in taxol-treated rats." Journal of Traditional and Complementary Medicine. 14(3):276–286. doi:10.1016/j.jtcme.2024.03.004.

121. a, bZhangM, ZhangH, JiaL, ZhangY, QinR, XuS, MeiY (2024). "Health benefits and mechanisms of theobromine." Journal of Functional Foods. 115:106126. doi:10.1016/j.jff.2024.106126.

122. a, bChenT, GeZ, YangX, WangX, ZuoH, LiaoY, ChenZ, ZhangZ, ChenM, ZhaoJ, LuoJ (2024). "Characterization of a new Camellia plant resource with low caffeine and high theobromine for production of a novel natural low-caffeine tea." Food Chemistry X. 23:101586. doi:10.1016/j.fochx.2024.101586.

123. a, b, c, dLiM-C, WangC-J (2024). "Association of Caffeine and Theobromine Intakes With Cognitive Function Performance in Older Adults." Current Developments in Nutrition. 8:103382. doi:10.1016/j.cdnut.2024.103382.

124. a, bBrehmJN, SorgJA (2024). "Theophylline-based control of repA on a Clostridioides difficile plasmid for use in allelic exchange." Anaerobe. 88:102858. doi:10.1016/j.anaerobe.2024.102858.

125. ^ZuniegaJ, GrabulosJ, LebrunM, AumondT, DanielC, FarrussengD, BratP (2024). "'Cavendish' banana crown rot control through sustained release of thymol by metal-organic frameworks (MOFs)." Postharvest Biology and Technology. 217:113119. doi:10.1016/j.postharvbio.2024.113119.

126. ^ZhaoC, SunL, ZhangY, ShuX, HuY, ChenD, ZhangZ, XiaS, YangH, BaoX, LiJ, XuY (2024). "Thymol improves ischemic brain injury by inhibiting microglia-mediated neuroinflammation." Brain Research Bulletin. 215:111029. doi:10.1016/j.brainresbull.2024.111029.

127. ^Gutiérrez-GonzálezP, Fernández-PeñaL, LuciaA, OrtegaF, RubioRG, GuzmánE (2024). "Aqueous Dispersions of Oleic Acid Nanodroplets for Thymol Encapsulation." Colloids and Surfaces a Physicochemical and Engineering Aspects. 690:133775. doi:10.1016/j.colsurfa.2024.133775.

128. a, bHuttunenJ, TampioJ, JärvinenJ, MontaserAB, Markowicz-PiaseckaM, HuttunenKM (2024). "Amino acid derivative of probenecid potentiates apoptosis-inducing effects of vinblastine by increasing oxidative stress in a cancer cell-specific manner." Chemico-Biological Interactions. 388:110833. doi:10.1016/j.cbi.2023.110833.

129. a, bXuZ, WangG, WangQ, LiX, ZhangG, QurbanA, ZhangC, ZhouY, SiH, HuL, WangF, WangY, TianZ, ChenW, Jin S, DingF (2023). "A near-complete genome assembly of Catharanthus roseus and insights into its vinblastine biosynthesis and high susceptibility to the Huanglongbing pathogen." Plant Communications. 4(6):100661. doi:10.1016/j.xplc.2023.100661.

130. ^MachetA, PoudouC, TomowiakC, GastinneT, GardembasM, SystchenkoT, MoyaN, DebiaisC, LevyA, GruchetC, SabirouF, NoelS, BouyerS, LeleuX, DelwailV, GuidezS (2022). "Hodgkin lymphoma and female fertility: a multicenter study in women treated with doxorubicin, bleomycin, vinblastine, and dacarbazine." Blood Advances. 7(15):3978–3983. doi:10.1182/bloodadvances.2021005557.

131. ^LuS, WangJ, HuangJ, SunF, ZhuJ, QueY, LiH, GuoY, CaiR, ZhenZ, SunX, ZhangY (2024). "Pegylated liposomal doxorubicin combined with cyclophosphamide and vincristine in pediatric patients with relapsed/refractory solid tumor: a single-arm, open-label, phase I study." EClinicalMedicine. 73:102701. doi:10.1016/j.eclinm.2024.102701.

132. a, bViinikainenK, IsohanniP, KanervaJ, LönnqvistT, LauronenL (2024). "Without ENMG, detecting pediatric vincristine neuropathy is a challenge." Clinical Neurophysiology Practice. doi:10.1016/j.cnp.2024.01.005.

133. a, bOhmuraK, KinoshitaT, TomitaH, OkadaH, ShimizuM, MoriK, TaniguchiT, SuzukiA, IwamaT, HaraA (2023). "Prevention of vincristine-induced peripheral neuropathy by protecting the endothelial glycocalyx shedding." Biochemical and Biophysical Research Communications. 691:149286. doi:10.1016/j.bbrc.2023.149286.

134. ^RazaviAC, RichardsonLC, CoronadoF, DzayeO, BhatiaHS, MehtaA, QuyyumiAA, VaccarinoV, BudoffMJ, NasirK, TsimikasS, WheltonSP, BlahaMJ, BlumenthalRS, SperlingLS (2024). "Aspirin use for primary prevention among US adults with and without elevated Lipoprotein (a)." American Journal of Preventive Cardiology. 18:100674. doi:10.1016/j.ajpc.2024.100674.

135. ^MeshksarS, JahromyMH, QomiM, SamiN, FaaliF (2024). "Formulation and evaluation of the effects of ophthalmic nanoemulsion of Nigella sativa seed extract on atropine-induced dry eye in mice." Phytomedicine Plus. 4(2):100541. doi:10.1016/j.phyplu.2024.100541.

136. ^LehouxT, PorcheCN, CapobiancoA, GervillaM, LecuyerF, AnthouardJ, WeinerL (2024). "Towards virtual reality exposure therapy for cocaine use disorder: A feasibility study of inducing cocaine craving through virtual reality." Addictive Behaviors Reports. 19:100549. doi:10.1016/j.abrep.2024.100549.

137. ^Suárez-GarcíaA, Álvarez-FreireI, Bermejo-BarreraAM, Cabarcos-FernándezP, Tabernero-DuqueMJ (2023). "Disappearance of codeine, morphine and 6-MAM in hair after cessation of abuse." Forensic Science International. 352:111855. doi:10.1016/j.forsciint.2023.111855.

138. a, bTadayonN, RamazaniA, RezazadehS, NohoojiMG, AngouraniHR (2024). "Isolation and investigation of antibacterial activities and cytotoxicity of atropine and scopolamine." Results in Chemistry. 10:101732. doi:10.1016/j.rechem.2024.101732.

139. ^Cid-PérezTS, Munguía-PérezR, Nevárez-MoorillónGV, Ochoa-VelascoCE, Navarro-CruzAR, Avila-SosaR (2024). "Carvacrol and thymol effect in vapor phase on Escherichia coli and Salmonella serovar Typhimurium growth inoculated in a fresh salad." Heliyon. 10(9):e29638. doi:10.1016/j.heliyon.2024.e29638.

140. ^HuinV, BlumD, DelforgeV, CailliauE, DjeziriS, DujardinK, GenetA, ViardR, AttarianS, BruneteauG, CassereauJ, GenestetS, KaminskyA-L, SorianiM-H, LefilliatreM, CouratierP, Pittion-VouyovitchS, EsselinF, De La CruzE, GuyN, KolevI, CorciaP, CintasP, DesnuelleC, BuéeL, Danel-BrunaudV, DevosD, RollandA-S (2024). "Caffeine consumption outcomes on amyotrophic lateral sclerosis disease progression and cognition." Neurobiology of Disease. 199:106603. doi:10.1016/j.nbd.2024.106603.

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