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Review Article

Biological Properties of Polyherbal Formulations: A Review of their Antimicrobial, Anti-Inflammatory, Antioxidant, and Toxicological Activities

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ABSTRACT

The use of traditional and folklore systems of medicine has been an important part of healthcare worldwide, and polyherbal formulations, which are combinations of different herbs, are gaining recognition for their medicinal and therapeutic potential. These formulations can be optimized to have stronger therapeutic effects with lower toxicity. The aim of this study was to review research on the antimicrobial, anti-inflammatory, antioxidant and toxicological properties of polyherbal formulations around the world, with a view to promoting their use and identifying areas where further research is needed. The author analyzed 99 articles published between 2010 and 2022, using scientific search engines such as Elsevier, BioMed Central, ScienceDirect, PubMed, and Scopus, to assess the use of polyherbal formulations in different countries. This article enlists some commercial and non-commercial polyherbal formulations all around the world with India leading in the number of publications on polyherbal formulations, followed by Nigeria, and Pakistan. The various pharmacological studies conducted have shown that polyherbal medicines possess antimicrobial, anti-inflammatory, antioxidant and toxicological properties, hence, validating their traditional use. However, further clinical work is required to fully understand the therapeutic potential of polyherbal formulations. The growing interest in the therapeutic use of non-toxic conventional medicinal plants as low-cost alternatives for disease prevention and treatment has made natural products valuable tools for creating new lead compounds and scaffolds. Plants will continue to play a pivotal role in the discovery of drugs for human diseases, and the development of potent cures derived from plants would represent significant progress in the treatment of diseases.

Key words: Antimicrobial, Anti-inflammatory, Antioxidant, Polyherbal medicines, Toxicological properties.

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INTRODUCTION

Throughout history, natural remedies made from herbs have been used to treat various physiological disorders, and are generally considered safe. According to the World Health Organization, around 80% of the global population relies on herbal-based products to treat different ailments.[1] The global market for herbal formulations is currently estimated at $1.5 billion and it is expected to expand significantly as demand for natural remedies used for preventing and curing different diseases increases.[1]

Herbs/herbal products are vital sources of novel pharmaceuticals because they contain a significant amount of secondary metabolites, such as alkaloids, flavonoids, isoflavonoids, lignans, quinones, catechols, coumarins, polyphenols, lectins, monoterpenes, and triterpenes which are accountable for the positive effects of the herbal products.[1,2] The quality and quantity of these bioactive compounds determine the therapeutic effectiveness of herbal formulations.[1] For instance, due to the abundance and diversity of the flavonoid and phenolic content of *Datura stramonium*, it has been reported to exhibit significant anti-inflammatory and antimicrobial activities.[3] *Argemone mexicana,* on the other hand, contains a lot of alkaloids and has traditionally been used to treat various dermatological disorders, warts, and inflammatory complications.[3] When monotherapy is inadequate to combat a clinical condition, traditional medicine employs polyherbal approaches.[4]

Polyherbal medicines, which contain two or more herbal ingredients are often more effective than single drugs because of their complementary and/or potentiating activities. The combination of two or more herbal extracts brings about increased therapeutic efficiency, enhanced pharmacological actions, faster relief, and reduced adverse effects as compared to conventional medicine due to a lower dose of administration.[1,2,4,5] Polyherbal medicines are now widely preferred and used around the world because of their high effectiveness, ready availability, low toxicity, and environmentally friendly nature, and it reduces the time of treatment or the individual cost of anti-inflammatory and antimicrobial drugs, resulting in lower prescription costs.[3,5] The concept of polyherbal combination has been well established and has achieved remarkable success in allopathic medicine, providing patients with new hope.[6]

Despite tremendous advancements in human medicine, infectious diseases caused by bacteria, fungi, viruses, and parasites remain a significant challenge to public health. These diseases are a major cause of morbidity and mortality in developing countries due to the relative scarcity of medicines and the emergence of widespread drug resistance to antimicrobials or antibiotics.[7] Previously unproven data on the antimicrobial activity of many plants have been scientifically verified, coinciding with an increase in records of pathogenic microorganisms

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resistant to antimicrobials. Therefore, plant-derived products can regulate microbial growth in a variety of circumstances. Despite the development of new antibiotics over the last three decades, the problem of microbial resistance to these drugs has increased. Bacteria are known to have the genetic ability to transmit and acquire resistance to drugs used as therapeutic agents,[8] which underscores the importance of discovering and developing novel pharmaceuticals.

Inflammation refers to the response of tissue to harmful stimuli such as physical injury, irritants, and pathogens. This response is identified by an increase in vascular permeability, alterations in blood flow, and migration of leukocytes to the affected regions.[9]

The five distinguishing characteristics of inflammation are tumour (swelling/oedema), colour (redness), dolour (pain), fever (warmth), and functio laesa (organ/tissue dysfunction).[10] The body responds to inflammation by releasing proinflammatory cytokines such as interleukins (IL-1β and IL-6), interferons (IFN), and tumour necrosis factor-alpha (TNF-α). These cytokines induce cyclooxygenase-2 (COX-2) which produces prostaglandins (PGs) leading to inflammation, swelling, and pain. Another inflammatory mediator, leukotrienes, is produced by the metabolism of arachidonic acids by lipoxygenase (LOX). Activation of macrophages results in the production of reactive oxygen species (ROS) which causes oxidative stress.[11]

Oxidative stress stimulates the release of proinflammatory cytokines and nitric oxide (NO) which exacerbate inflammatory diseases. Nitric oxide helps in the inhibition of mitochondrial enzymes and the activation of COXs in the production of PGs. Therefore, any substance or drug that inhibits COX-2, LOX, NO, and ROS can be useful in the prevention and treatment of inflammatory diseases.[11] To manage inflammation, there are numerous drugs available, however, the most commonly used are non-steroidal anti-inflammatory drugs (NSAIDs) such as diclofenac, indomethacin, naproxen, ketoprofen, and ibuprofen.[12] These drugs have limitations such as being palliative, inaccessible, unaffordable and having low efficacy, along with causing undesirable effects that may even be life-threatening.[9,13] Therefore, more research is needed to explore medicinal plants or polyherbal medicines as potentially effective therapeutic agents for inflammatory diseases.

Antioxidants play a crucial role in reducing cellular components' oxidation by molecular oxygen, preventing the chain reactions that result in the production of harmful free radicals like reactive oxygen species (ROS) and reactive nitrogen species (RNS). By removing free radical intermediates and inhibiting further oxidative reactions while being oxidized themselves, antioxidants are considered as important as nutraceuticals due to their many health benefits. They protect the body against oxidative stress linked to various chronic diseases and disorders. Antioxidants are any substance that, even in minute concentrations, can inhibit or delay the oxidation of a substrate or other molecules.[14] Therefore, antioxidants due to their ability to scavenge free radicals could potential be useful in the prevention and treatment of diseases linked to oxidants or free radicals. Phenolic acids, which are found in plants, have been shown to have a variety of biological effects, including antioxidant activity.[15] Antioxidant enzymes such as superoxide dismutase (SOD) and catalase act as defensive mechanisms by providing NADPH, which is required for the regeneration of glutathione (GSH) and protection against oxidative damage. Additionally, oxidative stress can lead to a decrease in glutathione S-transferase (GST) activity and a reduction in GSH content.[16]

The 2,2 diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assay is a commonly employed *in vitro* antioxidant assay used to determine the antioxidant potential of polyherbal extracts and in measuring the radical scavenging capability. The biological agent's ability to scavenge free radicals can be used to calculate antioxidant activity.[17] DPPH is a free radical having the strong ability to accept electrons to become a stable diamagnetic molecule. The potent DPPH radical scavenging activity of polyherbal formulation (PHF) has been attributed to its hydrogen-donating ability. The decrease in DPPH solution absorbance following the addition of PHF can be attributed to the strong reaction between the antioxidant-rich formulation and the DPPH solution. This reaction leads to the scavenging of the DPPH radical, which can be visualized by the colour change from purple to yellow in the DPPH solution upon the addition of PHF. The significant results of PHF in the DPPH *in vitro* antioxidant test indicate that it has a high reducing potential and can effectively scavenge free radicals.[18]

Furthermore, ABTS assay involves the generation of a blue/green chromophore resulting from the reaction between ABTS and potassium persulfate. This assay measures the relative ability of antioxidant compounds in plant extracts to scavenge the ABTS radical cation (ABTS), compared to standard quantities of synthetic antioxidant Trolox and the water-soluble vitamin E analogue.[5] Thus, antioxidants present in plants have potent properties for degenerating and scavenging harmful free radicals, such as ABTS.[5]

This study has reviewed all the research work conducted on antimicrobial, anti-inflammatory and antioxidant properties of polyherbal formulations in the past twelve year around the world. This is to validate and promote the use of polyherbal formulations, identify gaps in current knowledge and highlights area which more research is needed as well as to identified the herbal combination which can be used in the development of new pharmaceuticals.

Even though polyherbal remedies have reportedly been used for the management and treatment of various illnesses, concerns regarding their safety have been raised.[19] It is important to note that the quality, safety, and efficacy of polyherbal formulations can vary depending on the source and preparation method. Therefore, standardized formulations and proper quality control measures are necessary to ensure their safety and efficacy.

MATERIALS AND METHODS

The literature search was conducted from September 2022 to December 2022 and the study is based on a mixed-method review approach, which includes combining quantitative and qualitative research. A systematic comprehensive literature search was conducted on the following databases Google scholar, publishing sites such as Elsevier, JStor, Scopus, Science Direct, Cab Direct and BioMed Central (BMC), and PubMed. The databases and literature sources were chosen based on the topic covered and the main search and key terms included "polyherbal formulation", "antimicrobial", "anti-inflammatory", "toxicity" and "antioxidant activities". Search terms were set to be in the title, keywords, and abstract. The review focuses on work done on polyherbal medicine all over the world and the flow of study is shown in Figure 1.

RESULTS AND DISCUSSION

The therapeutic use of non-toxic conventional medicinal plants is gaining increasing attention as an alternative and cost-effective approach for the prevention and treatment of various diseases.[20] According to the World Health Organization, about 60–80% of the population in developing countries relies primarily on plants for their primary healthcare needs. The rise of herbal medicines has significantly increased foreign trade, and the global herbal medicine market is projected to hit approximately USD 117 billion by 2024.[21] For centuries, natural herbs and extracts have been utilized in both developed and developing countries to cure different ailments. Natural products have a distinct chemical richness, which results in a diversity of biological activities and drug-like properties; as a result, they have emerged as one

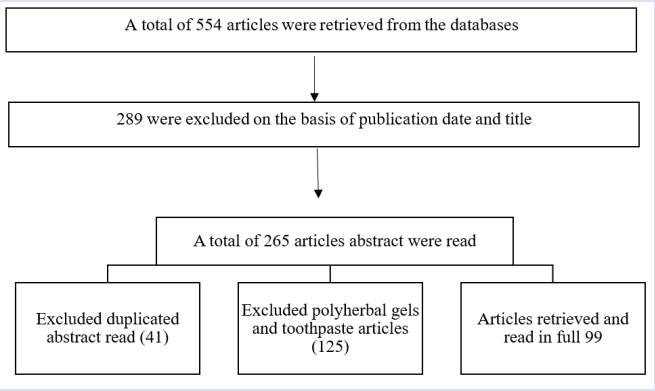

Figure 1: Flow of the study

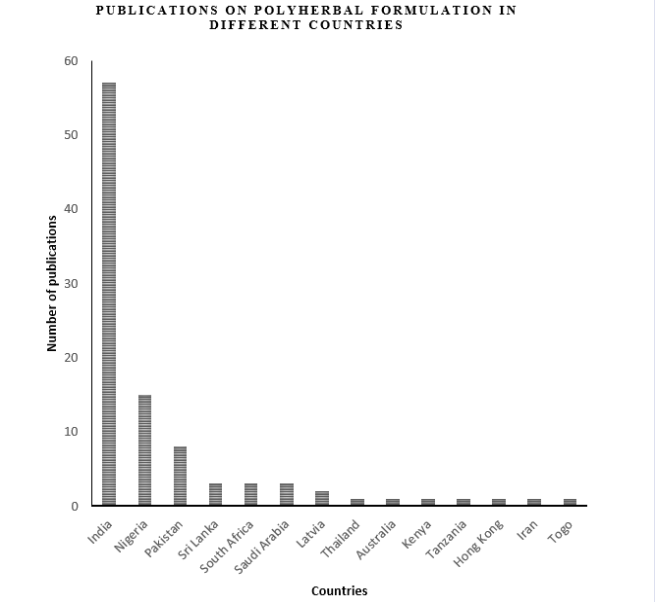

Figure 2: Publications on polyherbal formulation in different countries from 2010 till Dec 2022

of the most valuable tools for creating new lead compounds and scaffolds. These products will continue to be used in order to meet the urgent need for effective drugs development, and they will play a pivotal role in the discovery of drugs for the treatment of human diseases.[22] Moreover, synthetic antimicrobial agents available in the market exhibit certain drawbacks such as toxicity, low efficacy, the emergence of antimicrobial resistance, and high cost, which render them ineffective. Therefore, the development of a potent cure derived from plants would be a significant step forward in the treatment of microbial diseases.[23,24]

Polyherbal preparations, which are made from a combination of different medicinal plants, contain multiple bioactive constituents that interact with one another to achieve increased therapeutic effectiveness in the maintenance of human health.[25,26] They are used in the treatment of a wide range of diseases due to their broad therapeutic range and high efficacy, including diabetes, arthritis, liver and kidney disorders, cough, asthma, fever, respiratory disorders, and tuberculosis.[26c] It has been reported that polyherbal medicines possess antiviral, antibacterial, and antifungal activities.[25,27-30] This review reports that the polyherbal formulations exhibit significant antimicrobial, anti-inflammatory, and antioxidant activities (Table 1), and play a major role in the treatment and management of various diseases. The article lists some commercial and non-commercial polyherbal formulations all around the world and found that India has topped the number of publications on polyherbal formulations followed by Nigeria, and Pakistan (Figure 2).

Antimicrobial activity of polyherbal formulations

Based on ethnobotanical research, plants have been identified as a potential natural source of antimicrobial drugs that will provide novel or lead compounds that can provide unique or primary compounds to combat infections globally.[31] Various polyherbal medicines have been found to exhibit high antimicrobial activity due to the presence of alkaloids, phenols, glycosides, saponins, flavonoids, tannins, salicylic acid, and terpenes.[4,17,32-34] Tannins, for instance, are water-soluble polyphenols found in many plant foods and have been recognized as effective antibacterial agents against various pathogens. They have been reported to prevent the growth of microorganisms (fungi, yeasts, bacteria, and viruses) by precipitating microbial protein.[35,36] Tannins can deactivate enzymes that cause microbial adhesion, as well as hinder the movement of certain proteins. They also combine with polysaccharides to form a complex.[37] Similarly, flavonoids form a complex with either soluble or extracellular proteins and eventually bind to the bacterial cell wall. On the other hand, lipophilic flavonoids can considerably disturb the microbial cell membrane. Alkaloids are known to possess anti-tumour, analgesic, antispasmodic, and bactericidal potentials; Saponins are prominent for their anti-cancer, antioxidant, antimicrobial, and anti-inflammatory properties,[35,36] and steroids contain anti-inflammatory activity.[35] The antibacterial activity of these plant constituents is due to their ability to either block the production of the bacterial cell wall or disrupt the permeability of the cell membrane, ultimately resulting in the death of the microorganisms.[3,5]

Antibacterial agents work by inhibiting or regulating enzymes involved in cell wall biosynthesis, nucleic acid metabolism, and protein synthesis, a process known as translation inhibition. Another mechanism is membrane structure disruption, which causes changes in cellular functions. The majority of antibiotics are designed to reduce multiplication, thereby killing the organism. Some phytoconstituents in herbal formulations may bind to Gram-negative bacteria's membrane phospholipids and disrupt membrane integrity. Furthermore, it may inhibit peptidoglycan synthesis by blocking specific enzymes, thereby reducing the multiplication of bacteria and killing the organisms.[38]

The review findings revealed that the antimicrobial effectiveness of polyherbal formulations varied depending on the concentration and type of microorganisms tested. Some of the herbal remedies, such as THR-SK004, THR-SK010, and THR-SK011 used for the treatment of wounds demonstrated potent antibacterial activity against methicillin-resistant *S. aureus*, methicillin-susceptible *S. aureus* and *S. aureus* with MIC_{90} values of 4, 8 and 4 µg/mL respectively. This indicates that these herbal remedies meet the criteria proposed by Cos *et al.* (2006), which consider extracts with a selective activity and MIC values below 1–50 µg/mL as noteworthy. Also, polyherbal remedies such as Ambrex (8.7-23.4 µg/mL),[4] Ya-Sa-Marn-Phlae (4-32 µg/mL)[20], and KWTa, KWTb, KWTc, HBfs, HBts, AL, and FB (≤ 25 µg/mL)[39] had antimicrobial activities lower than 50 µg/mL, hence, they possess strong antimicrobial activity.

The majority of the polyherbal formulations demonstrated synergistic broad-spectrum antibacterial and antifungal activity, with MIC values ranging between 0.625–10 mg/mL. Some of the formulations, such as Ambrex, Chyawanprash, Plashbijadi churna, Vranahitkara ghruta, NOQ19, and Polyherbal nano colloids, *etc* exhibited antimicrobial activity comparable to the standard drugs. This suggests that these polyherbal remedies have the potential to be used as alternative treatments for bacterial and fungal infections. However, some polyherbal remedies such as Leone Bitters, Chandra Kalka, Sharkaradi Kalka, and Diakure did not possess any antimicrobial activity. This

Table 1: Antimicrobial, anti-inflammatory, antioxidant, and toxicological activities of polyherbal formulations.

S/N	Commercial name	Formulation with scientific names and plant part	Pharmacological activity		Bioassay models	Country	Reference
1.	Joshanda, used for the treatment of common cold	*Althea officinalis* (seed), *Cordia latifolia* (dried fruit), *Glycyrrhiza glabra* (dried rhizome), *Malva rotundifolia* (seed), *Onosma bracteatum* (leaf), *Viola odorata* (flower), *Zizyphus jujuba* (dried fruit)	Antimicrobial:	The findings revealed that the components of Joshanda (*Onosma bracteatum, Zizyphus jujuba,* and *Glycyrrhiza glabra* extracts exhibited strong activity against *S. aureus*; *Cordial latifolia* showed activity against *Hacmophillus influenae* while other plants do not inhibit the growth of the tested organisms.	*In vitro* activity	Pakistan	88
2.	THR-SK004, used for the treatment of wound infection	*Maranta arundinacea* (whole plant), *Oroxylum indicum* (bark), *Commelina benghalensis* (whole plant).	Antimicrobial:	The ethanol extracts of the herbal remedy had strong antibacterial potency against methicillin-resistant *S. aureus*, methicillin-susceptible *S. aureus,* and *S. aureus* at the MIC_{90} values of 4, 8, and 4 µg/mL respectively. However, none of the water extracts of the formulations displayed anti-staphylococcal activity.	*In vitro* antibacterial assay using broth microdilution method.	Thailand	50
3.	THR-SK010, used for wound healing	*Curcuma longa* (rhizome), *Areca catechu* (seed), *Oryza sativa* (seed), and *Garcinia mangostana* (pericarp).	Antimicrobial:	The ethanol extracts of the herbal remedies had strong antibacterial potency against methicillin-resistant *S. aureus*, methicillin-susceptible *S. aureus,* and *S. aureus* at the MIC_{90} values of 4, 8, and 4 µg/mL respectively. However, none of the water extracts of the formulations displayed anti-staphylococcal activity	*In vitro* antibacterial assay using broth microdilution method.	Thailand	50
			Anti-inflammatory:	The nitric oxide (NO) inhibitory results revealed that THR-SK010 ethanol extract exhibited NO production inhibition activity with IC50 value of 71.06, while the water extract was apparently inactive (IC50 > 100 µg/mL).	Inhibition of lipopolysaccharide induced nitric oxide production.		
			Anti-oxidant:	The result of ethanolic extract THR-SK010 showed the highest DPPH and hydroxyl radical scavenging activities with IC_{50} values of 19.24 and 13.58 µg/mL respectively.	2,2 diphenyl-1-picrylhydrazyl (DPPH) assay, hydroxyl free radical–scavenging activity and scavenging of superoxide radical.		
4.	THR-SK011, used for abscess treatment	*Ceiba pentandra* (leaf), *Aloe barbadensis* (leaf), *Coccinia grandis* (climber), *Senna siamea* (leaf), *Chromolaena odorata* (climber), *Tinospora crispa* (climber).	Antimicrobial:	The ethanol extracts of the herbal remedies had strong antibacterial potency against methicillin-resistant *S. aureus*, methicillin-susceptible *S. aureus,* and *S. aureus* at the MIC_{90} values of 4, 8, and 4 µg/mL respectively. However, none of the water extracts of the formulations displayed anti-staphylococcal activity	*In vitro* antibacterial assay using broth microdilution method.	Thailand	50
			Anti-inflammatory:	The nitric oxide (NO) inhibitory results revealed that THRSK011 ethanol extract exhibited NO production inhibition activity with IC50 value of 72.67 µg/mL, while the water extract was apparently inactive (IC50 > 100 µg/mL).	Inhibition of lipopolysaccharide induced nitric oxide production.		
			Anti-oxidant:	THR-SK011E possessed the highest superoxide radical scavenging activity, with an IC_{50} value of 75.00 µg/mL.	2,2 diphenyl-1-picrylhydrazyl (DPPH) assay, hydroxyl free radical–scavenging activity and scavenging of superoxide radical.		
5.	Polyherbal used for the treatment of vaginal infection.	*Azadirachta indica* (leaf), *Cichorium intybus* (leaf), and *Trigonella foenum-graecum* (seed).	Antimicrobial:	The hydroalcoholic extract of the remedy demonstrated synergistic broad-spectrum antibacterial and antifungal activity against *S. aureus*, *S. agalactiae*, *E. coli*, *C. albicans*, and *A. fumigatus* with the MIC values ranged between 5–7 mg/mL.	*In vitro* antibacterial assay using agar well diffusion method,	India	21

6.	Ambrex	*Withania somnifera* (root powder), *Orchis mascula* (seed endosperm), *Pistacia lentiscus* (resinous exudates), *Cycas circinalis* (male flowers) with amber a resin from *Pinus succinifera*.	Antimicrobial:	The aqueous extract of ambrex showed significant antibacterial activity against *P. putida*, *S. enterica*, *S. flexneri*, *S. paratyphi*, and *S. typhi* with the zone of inhibition ranging from 8.7-23.4 µg/mL which was comparable to the standards, streptomycin, and cifran with the zone of inhibition ranging from 12-25 µg/mL and 10-23 µg/mL respectively. Ambrex also exhibited potent inhibition of *C. albica*ns with a zone of inhibition of 7 µg/mL which is comparable to fluconazole 9 µg/mL.	*In vitro* evaluation using agar well diffusion method.	India.	4
7.	Chyawanprash (herbal tonic).	Prepared from 50 different herbs with *Emblica officinalis* as the basic ingredient. Other plants were not mentioned.	Antimicrobial:	The chloroform and hydrolyzed chloroform extracts of chyawanprash showed concentration-dependent antibacterial activity against *E. coli* and *S. aureus.*	*In vitro* antibacterial assay using the cup plate method.	India	89
8.	Plashbijadi churna	*Butea Monosperma* (seed), *Holarrhena antidysenterica* (seed), *Embelia ribes* (fruit), *Azadirachta indica* (seed), and *Swerita chirata* (whole plant).	Antimicrobial:	The remedy has been reported to exhibit antimicrobial activity.	-	India	90
9.	Vranahitkara ghruta used for the treatment of wounds.	*Berberis Aistata* (stem), *Azadirachta indica* (leaf), *Jasminum auriculatum* (leaf), *Pongamia glabra* (fruit/seed), *Picrorhiza kurroa* (rhizome), *Apis indica* (beeswax), *Trichosanthes dioica* (leaf), *Glycyrrhiza glabra* (root).	Antimicrobial:	The remedy has been reported to exhibit great antimicrobial activity.	-	India	23
10.	Aavarai Kudineer (antidiabetic formulation)	*Cassia auriculata, Cassia fistula, Syzygium jambos, Olax scandens, Saussurea lappa, Terminalia arjuna,* and *Cyperus rotundus.*	Antimicrobial:	The aqueous extract of Aavarai Kudineer was found to have antimicrobial activity against *B. subtilis*, *S. aureus, E. faecalis, P. aeruginosa, E. coli, K. pneumoniae* and fungal strains of *C. albicans* and *A. niger.*	*In vitro* antibacterial assay using disc diffusion method.	India.	91
			Antimicrobial:	The methanolic extracts of the remedy were significantly effective against *S. aureus, B. subtilis, E. coli,* and *P. aeruginosa* in a concentration-dependent manner.	Agar well diffusion and broth dilution method.		
11.	Polyherbal used for wound healing	*Plumbago zeylanica* (stem), *Datura stramonium* (leaf), and *Argemone mexicana* (aerial parts).	Anti-inflammatory:	When compared to normal and negative control animals, the polyherbal (2% and 5%) had a strong and maximal anti-inflammatory effect after 180 minutes of carrageenan injection.	*In vivo* experiment using Adult Wistar rats.	India.	3
			Toxicological:	The polyherbal was found to be safe up to a dosage of 2000 mg/kg, with no changes in the hair, skin, or behavior of treated animals. Also, there was no signs of skin irritation or adverse reaction in the rats.	*In vivo* assay using Adult Wistar rats.		
12.	KWTa, EL, KWTb, AL KWTc, HBfs HBss, HBts, and FB anti-tuberculosis remedies.	Prepared from 37 different herbs	Antimicrobial:	The result depicted that all the polyherbal remedies had anti-tubercular activity, with some showing more activity at concentrations less than 25 µg/mL. Also, the MIC values exhibited inhibitory activity against *M. tuberculos*is at 1.562 µg/mL. However, the control isoniazid exhibited more inhibitory activity at 0.05 µg/mL.	*In vitro* anti-*Mycobacterium tuberculosis* H37Rv using Middlebrook 7H9 media and MGIT BACTEC 960 system.	South Africa	39
13.	KWTa, EL, KWTb, AL KWTc, HBfs HBss, HBts, and FB anti-tuberculosis remedies	Prepared from 37 different herbs	Antimicrobial:	The study revealed that some of the polyherbal remedies showed antimicrobial activities against both bacterial and fungal isolates tested at the MIC value ranged of 1.25- 5 mg/mL.	Agar dilution method.	South Africa.	25

14.	Siddha polyherbal	*Asparagus racemosus* (leaf), *Syzygium aromaticum* (leaf), *Emblica officinalis* (leaf), and *Tinospora cordifolia* (leaf).	Antimicrobial:	The findings depicted that Siddha polyherbal extracts exhibited activity against *S. aureus, E. faecalis,* and *P. aeruginosa* at different concentrations ranging from 50-200 µg/mL	*In vitro* antibacterial assay by agar well diffusion method.	India.	26
15.	Qurs-e- afsanteen®	*Artemisia absinthium Valeriana officinalis Rheum emodi* Potassium nitrate and Ammonium chloride	Antimicrobial: Toxicological:	The remedy exhibited a significant zone of inhibition against the bacterial strains *B. subtilus* and *E. coli* with mean values of 21.38 and 15.93 respectively. The result showed that the Qurs-e-afsanteen® has less hemolytic activity with the mean valve of 12.89.	*In vitro* antibacterial assay by disc diffusion method. Cytotoxicity of the sample was determined by hemolytic activity.	Pakistan	17
16.	NOQ19 used for the treatment of Covid-19.	*Withania somnifera* (root), *Aegle marmelos* (leaf), *Glycyrrhiza glabra* (root), *Pluchea lanceolate* (leaf), *Adhatoda vasica* (leaf), *Piper longum* (Fruit), *Curcuma longa* (rhizome), *Cissampelos pareira* (root), *Phyllanthus fraternus* (plant), *Andrographis paniculate* (whole plant), *Alstonia scholaris* (stem bark), *Ocimum sanctum* (whole pant), and *Tinospora cordifolia* (stem).	Antimicrobial:	NOQ19 showed excellent antiviral efficacy eliminating 100% of the virus at the concentration of 0.9 mg/mL, while the IC_{50} of the drug was 0.2 mg/mL.	NOQ19 was tested on the infected African green monkey kidney epithelial cell Vero E6 (CL1008).	India.	24
17.	Thalipathiri chooranam used for the treatment of cough	*Glycyrrhiza glabra, Myristica fragrans, Zingiber officinale, Piper nigrum, Piper longum, Cuminum cyminum, Nigella sativa, Cinnamomum tamala, Saussurea lapa, Terminalia chebula, Terminalia belerica, Smilax china Acorus calamus, Balanophora fungosa,* and *Taxus beccata*	Antimicrobial: Anti-oxidant:	The study showed that the extracts exhibited significant antibacterial activity against *S. aureus, P. aeruginosa, K. pneumoniae* and *P. vulgaris,* with the highest activity of 14 mm zone of inhibition observed in *S. aureus*. The result revealed that nitric oxide radical scavenging of Thalipathiri Chooranam, increased gradually in a concentration-dependent manner, with a maximum reduction of 79.69±1.55 (100 µl). The maximum reducing power was at 100 µl (83.29±1.05) which resulted in the reduction of Fe^{3+} to Fe^{2+} by donating an electron. Thalipathiri Chooranam had scavenging range 79.69 at 100 µl which was higher than the positive control gallic acid 78.9±1.70 at 100 µl	*In vitro* antibacterial assay by disk diffusion method. Nitric oxide radical scavenging capacity and the reducing power activity of Thalipathiri Chooranam were determined by the spectrophotometric method.	India.	35
18.	Polyherbal antimicrobial (PHA)	*Azadirachta indica, Cichorium intybus,* and *Trigonella foenum-graecum* (TFG).	Antimicrobial:	PHA extract demonstrated synergistic broad-spectrum antimicrobial activities with minimum inhibition concentration between 5–7 mg/mL for both bacteria and fungi used.	The extracts were evaluated for antibacterial and antifungal activity by well diffusion assays.	India.	21
19.	Sagadevinei	*Vernonia cineria* (leaf), *Glycyrrhiza glabra* (root), *Santalum album* (bark), *Piper longum* (Fruit), *Hemidesmus indicus* (root), *Picro rhizakurroa* (whole plant), *Syzygium aromaticum* (Fruit), *Vettiveria zizanoides* (root), *Plectranthus vettiveroides* (root), and *Nymphaea pubesens* (stem).	Antimicrobial:	The remedy showed significant antibacterial potency at the concentration of 100 µL against *E. coli, P. aeruginosa, S. aureus, S. mutans, K. pneumonia.*	*In vitro* antibacterial assay by agar well diffusion method.	India.	92

20.	Triphala used for the management of metabolic disorders, dental and skin problems, and wound management etc	*Phyllanthus emblica* (fruit), *Terminalia bellerica* (fruit), and *Terminalia chebula* (fruit)	Antimicrobial:	The anti-infective assay revealed that Triphala formulation (TF) could reduce the virulence of all test pathogens at concentrations ranging from 0.5 to 100 g/mL. Worms challenged with TF-treated pathogens outlived those challenged with TF-untreated pathogens by 18-45.50%. Also, TF had no therapeutic effect on worms infected with *P. aeruginosa*, but had a significant effect on *C. violaceum* and *S. marcescens* infected worms. Only early treatment with TF was effective against *S. aureus*.	*In vivo* efficacy of Triphala was tested in the nematode host *Caenorhabditis elegans* N2-Bristol: anti-infective assay; post infection therapy and prophylactic.	India.	93
21.	Polyherbal formulation used for the treatment of urinary tract infection	*Brassica nigra* (seed), *Anetham graveolens* (seed), *Trachyspermum ammi* (seed), *Zingiber officinale* (rhizome), *Curcuma longa* (rhizome), *Ferula assa-foetida* (resins), *Piper nigrum* (seed) of both with and black pepper, *Acorus calamus* (stem), *Alpinia officinarum* (Rhizome), *Piper cubeba* (seed), *Nigella sativa* (seed), *Glycyrrhiza glabra* (stem), *Quercus infectoria* (fruit), *Myristica fragrance* (fruit), *Terminalia chebula* (fruit) and *Papaver somniferum* (seed)	Antimicrobial:	At the concentration of 10 mg/mL, PHF ethyl acetate and methanol extracts are active against UTI pathogens tested while the water extracts only inhibited the growth of *E. coli*. The ethyl acetate extract showed higher activity against *E. coli* with the zone of inhibition (ZOI) of 19 mm; MIC- 100 µg/mL; MBC- 125 µg/mL; and against *P. mirabilis* ZOI- 10.5; MIC- 375 µg/mL, and MBC- 400 µg/mL). The methanolic extract showed higher activity against *P. aeruginosa* (ZOI- 10.17 mm; MIC- 450 µg/mL; MBC- 475 µg/mL).	*In vitro* antibacterial assay by agar well diffusion method.	India.	5
			Anti-inflammatory:	At the concentration of 1 mg/mL, the extracts showed vital activity when compared with the standard Diclofenac (15.42). The maximum inhibition was found in water extract (36.54%), followed by ethyl acetate extract (33.27%), methanol (25.98%), and hexane extract (9.44%).	*In vitro* anti-inflammatory activity by membrane stabilization method.		
			Anti-oxidant:	In the DPPH assay, the maximum scavenging activity in terms of percentage of inhibition was observed in methanol extract (98.63%) and ethyl acetate extract (98.55%), whereas the minimum scavenging activity was observed in water extract (84.21%) and hexane extract (83.34%). The extracts showed higher activity in comparison with the natural antioxidant rutin (60.32), and the synthetic BHT (64.40) which probably marks the potential antioxidant capacity. The FRAP assay showed that the methanol extract had the highest reducing power activity of 117.67 ± 1.17 mM Fe (II) E/g extract followed by hexane extract (84.24 ± 1.61 mM Fe (II) E/g extract) and water extract (63.44 ± 2.78 mM Fe (II) E/g extract). PHA had higher radical scavenging activity in hexane extract (87.55 ± 5.62 µM TEAC/g) followed by water extract (24.08 ± 5.60 µM TEAC/g), ethyl acetate extract (12.88 ± 2.40 µM TEAC/g) and methanolic extract (12.35 ± 1.22 µM TEAC/g.	*In vitro* antioxidant by DPPH radical scavenging activity, Ferric reducing antioxidant power (FRAP) assay, and ABTS radical scavenging activity.		
22.	Shrishadi	*Albezzia lebbeck* *Cyprus rotandus* *Solanum xanthocarpum*	Antimicrobial:	Shrishadi possesses strong antimicrobial activity with the highest activity against *P. aeruginosa* and *C. parapsilosis* at 16 mg/mL and 15 mg/mL respectively.	*In vitro* analysis using disc diffusion method.	India.	33
23.	PHF used for the treatment of wounds	*Manilkara zapota* (leaf), *Tecoma stans* (leaf and flower), *Cassia fistula* (leaf and flower)	Antimicrobial:	At the concentration of 1000 µg/mL, the combination of *C. fistula* flowers and *C. fistula* leaf; *C. fistula* flowers and *M. zapota* leaf showed maximum ZOI of 23 mm and 21 mm for *S. aureus*; and 22 mm and 23 mm for *A. niger* respectively. The *C. fistula* flowers, *M. zapota* leaf and *C. fistula* leaf enhanced the antimicrobial nature more than the individual plants.	Antibacterial and antifungal activity using well diffusion assay.	India.	94

24.	Polyherhbal used in the treatment of skin diseases	*Azadirachta indica, Adhatoda vasica, Piper betle, Ocimum tenuiflorum* and *Pongamia pinnata*	Antimicrobial:	The results revealed that all the formulations viz. A, B, and C showed better ZOI ranging from 11.45 mm - 19.22 mm against *S. aureus, B. subtilis, A. niger,* and *E. coli* as compared with the control (8.98 mm - 9.76 mm).	*In vitro* antimicrobial activity by disc plate method.	India.	95
25.	AHPL/ AYCAP/0413 used for treatment of Acne	*Tinospora cordifolia, Rubia cordifolia, Hemidesmus indicus, Azardirachta indica, Acacia catechu* and *Solanum nigrum*	Antimicrobial:	The result revealed that 0.5 mL of the preparation had activity against *P. acnes, S. aureus, S. epidermidis* with ZOI of 18.33 mm, 19.20 mm, and 26.30 mm respectively, while the standard drug (clindamycin) was at 26.80 mm.	*In vitro* assay by agar well diffusion method.	India.	49
			Anti-inflammatory:	A significant reduction in paw oedema was observed in AHPL/AYCAP/0413 and Diclofenac groups as compared to the control group. The percentage inhibition of paw oedema for the AHPL/AYCAP/0413 and for standard Diclofenac sodium groups was 51% and 58% respectively.	*In vivo* experiment using carrageen-an-induced paw oedema in rats.		
26.	Gulgulupanchapa-la choornam used in healing wounds and skin diseases	*Commiphora wightii, Terminalia chebula, Terminalia bellirica, Phyllanthus emblica, Piper longum, Cinnamomum verum* and *Elettaria cardamomum.*	Antimicrobial:	The ethanol extract of choornam inhibited the growth of *S. aureus* and *P. aeruginosa*. The inhibitory zone of the extract was 2.1 cm against *P. aeruginosa* and 1.9 cm against *S. aureus* while ciprofloxacin showed an inhibitory zone of 3.1 cm against *P. aeruginosa* and 3 cm against *S. aureus.*	*In vitro* antibacterial assay by agar well diffusion method.	India.	60
			Anti-oxidant:	The extract also showed a dose-dependent ability to scavenge DPPH radicals thus establishing its antioxidant potential.	The antioxidant potential of the choornam was analyzed by DPPH assay.		
27.	DAS-77® effective in the treatment of piles, dysentery, cholera, menstrual pain, stomach disorder, ulcer, constipation, diarrhoea, and sexually transmitted infections	*Mangifera indica* (bark), and *Carica papaya* (root).	Antimicrobial:	The MIC of the extract against *S. aureus* and *E. coli* was at 100 mg/mL and 50 mg/mL respectively, while that of ciprofloxacin and tetracycline were at 50 µg/mL and 62.5 µg/mL, respectively. The extract did not show any inhibitory effect against *E. faecalis* and *P. aeruginosa*.	The antimicrobial activity using the agar-well diffusion method.	Nigeria	31
			Toxicological:	The result showed that DAS-77 was not toxic as no mortality and visible signs of toxicity were observed I the mice upon administration of DAS-77 up to 20 mg/kg. Writhing, grooming, increased locomotor activity, and convulsion were the behavioral manifestations observed with the intraperitoneally route.	*In vivo* assay using Mice.		
28.	Udhara vayuhara churna	*Piper longum, Zingiber officinalis, Elettaria cardamom, Plumbago zeylanica, Carum carvi, Acoruscalamus* and *Embilica officinalis.*	Antimicrobial:	The methanolic extract inhibited the growth of one or more test pathogens than the aqueous extract.	-	India.	96
29.	Diakure used in the treatment of diabetes	*Vetiveria zizanoides* (root), *Hemidesmus indicus* (rhizome), *Strychnos potatorum* (seed), *Salacia reticulata* (bark), *Holarhena antidysenterica* (seed), *Cassia auriculata* (bark), *Trigonella graecum* (seed) and *Acacia catechu* (bark).	Antimicrobial:	The result depicted that DiaKure fails both the antibacterial and anti-fungal activity tests.	*In vitro* antimicrobial by cup plate method and filter paper disk method.	India.	97
30.	Ativishadi churna used in the treatment of diarrhea.	Ativisha (root), Kutaz (stem bark) and Indrayava (seed)	Antimicrobial:	The result showed that Ativishadi Churna possesses activity against *E. coli* and *Salmonella* spp.	*In vitro* antibacterial by using disk diffusion method.	India.	98
31.	Nalpamaradi Keram	*Ficus benghalensis, Ficus racemose, Ficus religiosa* and *Ficus microcarpa*	Antimicrobial:	The remedy was found to possess activity against *S. aureus* with the ZOI of 20.0 mm.	Agar-well diffusion method.	India.	15

32.	PHF used against gastrointestinal diseases.	Made from a total of 25 plants species to form 14 polyherbal recipes.	Antimicrobial:	The polyherbal remedies showed activity against both tested fungal and bacterial isolates with the inhibition zone ranging from 19.67 mm - 30 mm. Some of the polyherbal recipes have enhanced antimicrobial potential with better efficacy than tested antibiotics.	Agar well diffusion method.	Pakistan.	6
33.	PH combination	*Withania somnifera, Bacopa monnieri,* and *cinnamomum zeylanicum*	Antimicrobial:	The Polyherbal formulation showed moderate to mild antibacterial activity against most of the tested bacteria.	*In vitro* antibacterial by the cup and plate method.	Australia	99
			Anti-oxidant:	The reducing power of the extract increased with the concentration.	Antioxidant activity was determined by Ferric ion-reducing antioxidant power assay.		
34.	Polyherbal cream used for the treatment of skin diseases	*Cyperus brevifolius* (root), *Asparagus gonoclados* (rhizome), and *Psidium guajava* (leaf)	Antimicrobial:	The results showed that the polyherbal extracts showed significantly higher antibacterial activity (50 mg/mL) against the tested pathogenic bacterial strains. Also, both the 10% and 20% creams were active *S. aureus, B. subtilis, E. coli,* and *P. aeruginosa,* with MICs of 12.5, 12.5, 25, and 50 mg/mL, respectively.	Agar disc diffusion and agar well diffusion assay.	Sri Lanka	100
			Anti-oxidant:	The antioxidant activity of the 20% ointment samples was higher than the 10% ointment samples. The reducing power increased with the increased concentration.	Antioxidant activity was determined by Ferric ion-reducing antioxidant power assay.		
35.	AHPL/ AYTOP/0213 cream used for the treatment of Acne.	*Berberis aristata, Symplocos racemose, Glycyrrhiza glabra, Myristica fragrans, Rubia cordifolia, Acarus calamus, Coriandrum sativum,* and *Salmalia malabarica.*	Antimicrobial:	The cream inhibited the growth of *P. acnes, S. epidermidis* and *S. aureus* with the ZOI of 20.68, 28.20, and 21.40 mm respectively, which was comparable to clindamycin. The overall MIC of the cream was observed at 2.5 mg/mL.	Agar well diffusion method.	India.	101
			Anti-inflammatory:	The result revealed that there was a significant reduction in rat paw oedema (43%) with AHPL/AYTOP/0213 which was also comparable to diclofenac sodium cream (56.09%).	*In vivo* experiment using carrageen-an-induced paw oedema in rats.		
			Toxicological:	The findings showed that the rat's skin where AHPL/AYTOP/0213 cream was applied showed no erythema or edema, and the primary skin irritation index of the cream was calculated as 0.00.	*In vivo* assay using Wistar albino rats.		
36.	Chandra Kalka used for the treatment of respiratory disorders of paraplegia disease and congestion. Sharkaradi Kalka used for the treatment of fever in children as well as, cough, asthma conditions and constipation.	A total of 31 medicinal plants are used to prepare the Chandra Kalka and 18 are used in the preparation of the Sharkaradi Kalka	Antimicrobial:	Both PHF do not possess antibacterial activity at the concentration of 1 mg/mL against *E. coli, S. aureus, B. subtilis,* and *S. epidermidis.*	Agar well diffusion method.	Sri Lanka	51
			Anti-inflammatory:	Both formulations showed moderate anti-inflammatory activity as they were able to stabilize the erythrocyte membranes.	Anti-inflammatory activity was determined using a human red blood cell membrane stabilization assay.		
			Anti-oxidant:	Both remedies possess antioxidant activity, however, the radical scavenging ability of Sharkaradi Kalka (133.19 µL/mL) was higher than Chandra Kalka (388.10 µL/mL), but has a lesser activity compared to L-Ascorbic acid (10.97 µL/mL).	Antioxidant activity was evaluated using the DPPH radical scavenging assay.		
37.	PHF	*Wedelia chinensis* (leaf) and *Oerhaavia diffusa* (root).	Antimicrobial:	The results showed that the formulation possesses antibacterial activity at the concentration of 5 mg/mL against *E. faecalis, S. aureus, K. pneumonia*, and *P. aeruginosa.*	*In vitro* antibacterial activity using agar well diffusion method.	India.	102
			Anti-oxidant:	The results showed that the formulation possesses a better scavenging effect at lower concentrations (100 µg/mL). The FRAP assay reveal that the mixture showed dose depended on an increase in concentration with maximum absorption of 0.767 at 300 µg/mL.	DPPH radical scavenging assay and FRAP assay.		

38.	HAE-LVR05	*Phyllanthus niruri* (leaf), *Azadirachta indica* (leaf), *Picrorhiza kurroa* (Rhizome), *Eclipta alba* (whole plant) and *Swertia chirata* (stem and leaf).	Antimicrobial:	The results showed that HAE-LVR05 possesses antibacterial and antifungal activity. The formulation was effective in *S. typhimurium* with the ZOI of 15.40 mm at 500 µg/mL; and 12.17 mm at the concentration of 500 µg/mL in *C. albicans.*	*In vitro* antimicrobial activity by disc diffusion method.	India.	38
39.	PHF	*Karanj Beej Oil, Jafi, Neem, Sariva sativa, Glycyrrhiza glabra, Rubia cordifolia,* and *Patol patra.*	Antimicrobial:	The PHF had significantly higher antibacterial activity than the control group. PHF inhibited *E. coli* (2.5 mm), *K. aerogenes* (2 mm), *P. aeruginosa* (1 mm), and *P. vulgaris* (1.5 mm) with a mild-to-moderate zone of inhibition.	Agar well diffusion method.	India	40
			Anti-oxidant:	The PHF exhibited the antioxidant activity of 90% at 100 ug/mL, whereas ascorbic acid was found to be 75.16 at 100 ug/mL. The IC_{50} value of the PHF and ascorbic acid was found to be 3.118 ug/mL and 23.32 ug/mL, respectively.	2, 2-diphenyl-1-picrylhydrazyl DPPH radical scavenging method.		
40.	PHF	*Vetiveria zizanioides, Trichosanthes cucumerina,* and *Mollugo cerviana*	Antimicrobial:	The PHF was found to be highly effective against *E. coli, S. aureus, P. aeruginosa, P. mirabilia, B. subtilis* and *Enterbacter* sp., with the ZOI measured to be 33 mm, 17 mm, 22 mm, 40 mm, 33 mm, and 38 mm, respectively.	*In vitro* antibacterial by disc diffusion method.	India.	37
			Anti-oxidant:	The antioxidant activity increased in a dose-dependent manner varying between 49% (20 µg/mL) and 95.3% (100 µg/mL).	DPPH radical scavenging assay.		
			Toxicological:	The methanol extract of polyherbal fraction showed cytotoxicity against the two cell lines with the LC_{50} value 467 ± 2.9 mg/ml against HeLa cell line and >800 mg/ml against MCF-7 cell lines.	The extract was tested against HeLa and MCF cell lines.		
41.	Entoban syrup used for the treatment of acute gastrointestinal infections.	*Aegle marmelos* (unripe fruit/pulp), *Holarrhena antidysenterica* (bark), *Berberis aristata* (black fruit), *Butea frondosa* (leaf), *Quecrus infectoria* (gall) and *Myrtus communis* (berries).	Antimicrobial:	The syrup inhibited the growth of *S. aureus, S. enterica, E. coli, S. dysenteriae, P. aeruginosa,* and *V. cholerae* with the ZOI measured to be 18.25 mm, 22 mm, 19 mm, 18.5 mm, 18.25 mm, and 19 mm, respectively.	Agar well diffusion method.	Pakistan.	103
42.	PHF used in the treatment of superficial infections.	PHF used in the treatment of superficial infections. *Terminella chebula* (fruit), *Terminella bellerica* (fruit) and *Emblica officinalis* (fruit).	Antimicrobial:	The PHF showed antimicrobial activity with the zones of inhibition greater than 10 mm against *T. rubrum, M. gypseum, C. albicans, M. furfur, S. aureus* and *S. pyogenes.*	Agar well diffusion method.	Sri Lanka	104
43.	Triple bark formulation used in wound healing.	*Acacia catechu* (bark), *Azadirachta indica* (bark) and *Szyzgium cumini* (bark).	Antimicrobial:	The results showed that the formulation has higher activity against *S. aureus, C. albicans, P. aeruginosa, E. coli, S. typhi* when compared with the control, Streptomycin sulphate.	Agar well plate method.	India	41
			Anti-oxidant:	At low concentrations, the formulation showed less DPPH scavenging activity, but at 100 µg/mL the PHF reduced 91% of DPPH (IC_{50} 29.03 µg/mL) which was comparable with ascorbic acid (94%) IC_{50} 15.52 µg/mL. The hydrogen peroxide scavenging ability of the extract was found to be higher (IC_{50} 20.88 µg/mL) than the ascorbic acid (19.81 µg/mL).	DPPH and hydrogen peroxide scavenging methods.		
			Toxicological:	The result showed that the formulation helps in the proliferation of fibroblast cells without affecting the viability.	Cytocompatibility of the formulation was studied on mouse 3T3 fibroblast cells using MTT assay.		
44.	Herbal formulation for mastitis treatment	*Aloe vera* and *Curcuma longa*	Antimicrobial:	The extracts exhibited potential antimicrobial activity against the tested microorganisms.	Agar well diffusion method.	India.	105

45.	Polyherbal remedy used for the management of peptic ulcers.	*Rhynchosia recinosa* (aerial parts), *Ozoroa insignis* (stem bark), *Maytenus senegalensis* (stem bark), *Entada abyssinica* (stem bark) and *Lannea schimperi* (stem bark).	Antimicrobial:	The remedy exhibited antimicrobial activity against *E. coli, S. typhi, V. cholerae* and *K. pneumoniae* with MICs between 0.8 – 12.5 mg/mL.	*In vitro* antibacterial assay using the microdilution method.	Tanzania	106
			Toxicological:	The formulation showed very low acute toxicity in mice and in the brine shrimp lethality test. The ethanol extracts of the remedy gave an LC_{50} value of 66.12µg/ml. The formulation was well tolerated during the 14-day observation period and at doses up to 5000 mg/kg body wt.	*In vitro* assay using brine shrimp lethality test and i*n vivo* using Sprague Dawley rats.		
46.	Jatyadi Thailam (JT_{YG}) used for the treatment of chronic wound.	*Aerva lanata* (whole plant), *Calycopteris floribunda* (leaf), *Curcuma longa* (rhizome), *Cynodon dactylon* (whole plant), *Erythrina variegate* (leaf), *Glycyrrhiza glabra* (root), *Jasminum flexile* (leaf), *Murraya koenigii* (leaf), *Nigella sativa* (seed), *Oldenlandia corymbose* (whole plant), *Physalis minima* (whole plant), *Pupalia atropurpurea* (whole plant), *Vitex negundo* (leaf).	Antimicrobial:	The antibacterial activity of Jatyadi extracts was higher against Gram-positive bacteria (*S. aureus*, MRSA, *S. epidermidis and E. faecalis*), with the MICs varying from 1.95 to 62.5 mg/mL. However, the Gram-negative bacteria (*E. coli*, *P. aeruginosa*, MDR *P. aeruginosa*, *P. mirabilis*, and *K. pneumoniae*) were only susceptible to ethanol extracts of Jatyadi.	Agar disk diffusion test and the E-test.	Latvia	107
			Anti-inflammatory:	Jatyadi extracts efficiently inhibited in a dose-dependent manner the mRNA expression and protein secretion of proinflammatory cytokines IL-6 and IL-1β, and chemokines MCP-1 and CXCL10 in LPS-challenged macrophages. Hence, Jatyadi extracts could be used to normalize overexpressed cytokines in chronic wounds and, could shorten prolonged inflammation.	Gene expression of inflammatory cytokines and chemokines in THP-1 Macrophages.		
47.	Jatyadi Ghritam (JT_{AFI}).	*Azadirachta indica* (leaf), *Chrysopogon zizanioides* (root), *Berberis aristate* (stem), *Curcuma longa* (rhizome), *Glycyrrhiza glabra* (root), *Hemidesmus indicus* (root), *Jasminum officinale* (leaf), *Picrorhiza kurroa* (root/rhizome), *Pongamia pinnata* (seed), *Rubia cordifolia* (root), *Trichosanthes dioica* (leaf).	Antimicrobial:	The antibacterial activity of Jatyadi extracts was higher against Gram-positive bacteria (*S. aureus*, MRSA, *S. epidermidis and E. faecalis*), with the MICs varying from 1.95 to 62.5 mg/mL. However, the Gram-negative bacteria (*E. coli*, *P. aeruginosa*, MDR *P. aeruginosa*, *P. mirabilis*, and *K. pneumoniae*) were only susceptible to ethanol extracts of Jatyadi.	Agar disk diffusion test and the E-test.	Latvia.	107
			Anti-inflammatory:	Jatyadi extracts efficiently inhibited in a dose-dependent manner the mRNA expression and protein secretion of proinflammatory cytokines IL-6 and IL-1β, and chemokines MCP-1 and CXCL10 in LPS-challenged macrophages. Hence, Jatyadi extracts could be used to normalize overexpressed cytokines in chronic wounds and, could shorten prolonged inflammation.	Gene expression of inflammatory cytokines and chemokines in THP-1 Macrophages.		
48.	Jatyadi thailam (JT_{AFI} & JT_{YG}) used for the treatment of inflammation related ailment specifically non-healing chronic foot ulcers.		Antimicrobial:	The test organisms showed susceptibility to both formulations with AFI and YG having MIC values ranging from 0.156 to 1.250 mg/mL. The remedies exhibited the best antibacterial activity against *S. aureus* (0.312 mg/mL) and antifungal activity against *A. fumigatus* (0.156 mg/mL). AFI had MIC values of 0.312 mg/mL against *A. flavus, C. neoformans*, and *C. albicans*.	*In vitro* antibacterial assay by broth microdilution method.	India.	108
			Anti-inflammatory:	Both formulations exhibited significant dose-dependent anti-denaturation and anti-proteinase activities with AFI exhibiting maximum inhibition of 91.05% and YG (52.24%) at the concentration of 2500 µg/mL while the standard drug aspirin showed 95.53% inhibition of protein denaturation at its lowest concentration of 500 µg/mL. The thailam also showed marked stabilization of the human red blood cell membrane against thermal hemolysis and inhibited heat-induced hemolysis more effectively in a dose-dependent manner.	*In vitro* anti-inflammatory activity was determined by assaying albumin denaturation inhibition, membrane stabilization (hypotonicity-induced hemolysis), heat-induced hemolysis and antiproteinase activities.		

49.	Leone Bitters used as an appetite stimulant and stomachic.	*Parinari curatellifolia* (seed), *Cocos nucifera* (root) and *Gongronema latifolia* (stem).	Antimicrobial:	Leone Bitters do not possess antimicrobial activity at the concentration used.	*In vitro* antimicrobial using the cup diffusion method.	Nigeria.	86
			Toxicological:	The acute toxicity study showed 80% death for all the animals that received 20.0 g/kg bwt of the extract and 42.8 % and 14.3 % for animals that received 15.0 g and 10.0 g respectively, while there was no death in the animals that received 5.0 g/kg bwt and less. Decrease in the body weight was observed in rats that received higher doses, no morphological changes in the colour of the organs however, the histological result revealed that at the dose of 500 mg/kg bwt, the drug may have affected the sperm production rate in the testis. Also, no abnormality was observed in the tissue morphology of the liver, kidney and heart. However, there was significant changes in the various organs' weights especially in kidney, liver and brain in the animals.	*In vivo* assay using Swiss albino mice and Wistar rats.		
50.	PHF-M1	*Diploclisia glaucascens, Murraya koenigii, Ocimum tenuiflorum* and *Curcuma longa.*	Antimicrobial:	The findings revealed that PHF-M1 extract possesses considerable amount of antimicrobial inhibition against mastitis causing pathogens with the MIC values ranging from 24±0.58 to 12.33±0.33.	*In vitro* antimicrobial using agar diffusion method.	India.	77
			Toxicological:	The results of the acute oral toxicity test showed that PHF-M1 did not exhibit any toxicity at dose rates of 5, 50, 300, and 2000 mg/kg. The animals in the study showed no signs of ill health and their food and water intake remained normal. No behavioral changes were observed during the study period.	*In vivo* assay using Wistar rats.		
51.	Forty-six herbal branded products	-	Antimicrobial:	The result depicted that only nine of the herbal preparations exhibited better antimicrobial activities, while the rest of the formulations had no activity.	*In vitro* antimicrobial using well diffusion method	Pakistan	109
52.	Acnovin Capsule	Mahamajishthadi kwath, Panch neem churna, Sariva, Sonamukhi, Khadir twak, Haridra, AmLa, Bibhitaki, Haritaki and Gandhak rasayana	Antimicrobial:	The result showed that the extract possesses considerable amount of antibacterial activity against test isolates with the ZOI values ranging from 5-31 mm.	*In vitro* antibacterial assay using agar well diffusion method	India	28
53.	Ya-Sa-Marn-Phlae used for the treatment of wound	*Curcuma longa* (rhizome), *Areca catechu* (seed), *Oryza sativa* (seed), and *Garcinia mangostana* (pericarp).	Antimicrobial:	The result showed that Ya-Sa-Marn-Phlae exhibited a potent antibacterial activity against all tested staphylococcal isolates (*S. aureus*, *S. epidermidis*, bovine mastitis-isolated coagulase-positive staphylococci and coagulase-negative staphylococci) with MIC values ranging between 4-32 µg/mL. At 4x MIC, the remedy was able to kill the tested organisms at approximately 2–4 log reduction within 2 h. Ya-Sa-Marn-Phlae inhibited the biofilm formation of the bacteria on polystyrene surfaces up to 48 h with a weak growth inhibition effect.	*In vitro* antibacterial assay using broth microdilution method. Biofilm formation was carried out in a flat-bottomed 96-well polystyrene microtiter plate	Thailand	20

54.	PHF used for the treatment of dysentery	*Camellia sinensis* (leaf), *Citrus lemon* (fruit), *Terminalia chebula* (fruit) extract along with Cinnamon, and Thyme oil	Antimicrobial:	The ZOI of the antimicrobial efficacy of the formulation was found to be 24 mm, 25 mm, and 25 mm; and the MIC values of 1.5 mg/mL, 1.5 mg/mL, and 2.0 mg/mL against *S. flexneri, S. enterica*, and *E. coli* respectively. Also, the results show that the polyherbal formulation significantly reduced biofilm formation by 67.94%, 65.56%, and 51.94% in the presence of 0.8 mg/mL formulation against *S. flexneri, S. enterica*, and 0.9 mg/mL against *E. coli* when compared to the control.	*In vitro* assay by well-diffusion method and broth dilution method The biofilm inhibition activity was determined on 96 well-polystyrene plates	India	75
			Toxicological:	The result depicted that different concentrations (5 mg/kg, 50 mg/kg, 300 mg/kg, and 2000 mg/kg) of PHF administered did not produce any significant changes in behavior, postural abnormalities, impairment in food and water intake, and loss or yellowing of hair. No mortality of animals was also observed.	*In vivo* assay using albino rats		
55.	Polyherbal nanocolloids (PHNc) used in the treatment of mastitis.	*Syzygium aromaticum, Cinnamomum verum, Emblica officinalis, Terminalia belerica, Terminalia chebula,* and *Cymbopogon citratus*	Antimicrobial:	The result showed that PHNc possesses more antibacterial activity than Ampicillin (25 µg) at the various concentrations of 25 µg, 50 µg, and 100 µg. At 100 µg of PHNc, a maximum ZOI of 27 mm was observed against *A, baumannii*, followed by *A. junii, K. pneumoniae,* and *P. stutzeri* which was 23 mm for each strain. The bactericidal concentrations of PHNc were 12.5 µg/mL for *A. junii* and *K. pneumoniae* and 6.25 µg/mL for *P. stutzeri* and *A. baumannii*..Also, biofilm formation was reduced in a dose-dependent manner. The average inhibition potential rates of PHNc for 6.25 µg/mL, 12.5 µg/mL, 25 µg/mL, and 50 µg/mL were found as 60%, 69%, 78%, and 88% for *A. junii, K. pneumoniae, P. stutzeri*, and *A. baumannii*, respectively at 48 h post-treatment.	*In vitro* antibacterial assay using agar well diffusion method. The biofilm inhibition activity was determined on 96 well-polystyrene plates	India	110
56.	Khoi-San	*1 Tulbaghia violacea, Alepidea longifolia, Cissampelos capensis, Glycyrrhiza glabra, Stoebe fusca* *2 Glycyrrhiza glabra, Helichrysum felinum, Alepidea longifolia, Elytropappus rhinocerotis, Dodonaea viscosa* *3 Eucalyptus globulus, Agathosma crenulata, Dodonaea viscosa* *4 Glycyrrhiza glabra, Helichrysum felinum, Agathosma crenulata, Tulbaghia violacea* *5 Alepidea amatymbica, Alepidea longifolia, Tulbaghia violacea, Curtisia dentata* *6 Eucalyptus globulus, Cinnamomum camphora, Glycyrrhiza glabra, Tulbaghia violacea, Alepidea amatymbica, Alepidea longifolia, Agathosma crenulata, Hypoxis hemerocallidea*	Antimicrobial:	Only the methanol extract of sample 3 showed the best antibacterial activity with MIC values of 49 µg/mL for *S. aureus* and *B.subtilis*, and 98 µg/mL for *K. pneumoniae* and *E. coli*.	*In vitro* antibacterial assay using microdilution method	South Africa	30

57.	PF-3	*Moringa oleifera, Viola odorata, Allium sativum*	Antimicrobial:	PF-3 showed a high zone of inhibition at the concentration of 200 mg/mL against *S. aureus* (18.8 mm), *S. typhi* (10.6 mm), *B. subtilis* (15.3 mm), *E. coli* (13.86 mm), *A. niger* (12.5 mm) and *C. albicans* (7.6 mm).	Agar well diffusion method	India	27
58.	Polyherbal Siddha formulation	*Gymnema sylvestre* (leaf), *Syzygium cumini* (seed), *Tinospora cordifolia* (stem), *Coccinia grandis* (leaf), *Trignonella foenum graecum* (seed), *Curcuma longa* (rhizome), *Andrographis paniculata* (leaf), *Catharanthus roseus* (leaf), *Terminalia bellirica* (fruit), *Phyllanthus emblica* (fruit), *Terminalia chebula* (fruit), *Salacia oblonga* (root), *Cassia auriculata* (flower).	Antimicrobial:	At the concentration of 10 mg/mL, the acetone and ethanol extracts of the formulation exhibited antibacterial activity with the zone of inhibition of 14 mm and 12 mm against K. *pneumonia,* 13 mm and 14 mm against *E. coli* and 12 mm against MRSA strain, respectively.	Agar well diffusion assay	India	29
59.	IBS-20 used for the treatment of irritable bowel syndrome	*Angelica dahurica* (root), *Artemisia scoparia* (aerial part), *Atractylodes macrocephala* (rhizome), *Aucklandia lappa* (root), *Bupleurum chinense* (root), *Citrus reticulata* (ripe fruit pericarp), *Codonopsis pilosula* (root), *Coix lacryma-jobi* (ripe kernel), *Coptis chinensis* (rhizome), *Fraxinus rhynchophylla* (banch or stem bark), *Glycyrrhiz uralensis* (root and rhizome), *Magnolia officinalis* (root, branch and stem bark), *Paeonia lactiflora* (root), *Plantago asiatica* (ripe seed), *Phellodendron amurense* (bark), *Pogostemon cablin* (aerial part), *Poria cocos* (sclerotium), *Saposhnikovia divaricate* (root), *Schisandra chinensis* (ripe fruit), *Zingiber officinale* (prepared rhizome)	Anti-inflammatory:	The results showed that IBS-20 has potent anti-inflammatory effects on innate immune cells *in vitro* as well as on murine model of colitis *in vivo.* The remedy inhibited LPS- or IFNΓ-stimulated expression of pro-inflammatory cytokines, classically activated macrophage marker nitric oxide synthase 2, and attenuated the IFNΓ-induced drop in transepithelial electric resistance, an index of permeability, in fully differentiated Caco-2 monolayer. In addition, it suppressed significantly the up-regulation of key inflammatory cytokines in inflamed colon from TNBS-treated mice	*In vitro* and *In vivo* experiment using mice	Hong Kong	48
60.	Phytexponent used to treat pain and inflammation	*Viola tricolor, Echinacea purpurea, Allium sativum, Matricaria chamomilla, Triticum repens*	Anti-inflammatory: Toxicological:	The result showed that the remedy exerted significant ($P < .05$) anti-inflammatory effects in carrageenan-induced paw oedema mouse model in a time-dependent manner, with significantly higher efficacy at 250 mg/Kg BW, than indomethacin (4 mg/Kg BW) The result depicts that phytexponent was not toxic to Vero E6 cells (CC_{50} >1000 µg/ml) compared to the control cyclophosphamide (CC_{50}=2.48 µg/ml).	*In vivo* experiment using Swiss albino mice *In vitro* assay in Vero E6 cell line	Kenya	9
61.	*Bhāraṅgyādi*	*Clerodendrum serratum*, *Hedychium spicatum* and *Inula racemosa*	Anti-oxidant:	The result suggests that the polyherbal formulation is a good potential for antioxidant activity as the reducing power showed a dose-depended increase in concentration with maximum absorption of 0.67 at 1000 µg/mL compared with Quercetin 0.856 µg/mL. ABTS assay depicted maximum inhibition of 64.2 with EC_{50} 675.31. Superoxide free radical shows a maximum scavenging activity of 62.45 with EC_{50} 774.70. Anti-lipid peroxidation free radicals scavenged maximum absorption of 67.25 with EC_{50} was 700.08.	The total reducing power, in vitro antioxidant activity by ABTS, Superoxide anion scavenging activity and lipid peroxidation assays.	India	111

62.	PHF	*Nyctanthes arbor-tristis* (leaf), *Aegle marmelos* (unripe and ripe fruit pulp), *Musa paradisiaca* (flower)	Anti-oxidant:	The result showed that the PHF exhibited better DPPH radical scavenging activity with an IC_{50} value of 71.5708 µg/mL than individual plants. In addition, a dose-dependent reducing power was observed, and it exhibited a higher reducing power of 63.67 µg/mL.	DPPH radical scavenging activity and Ferric ion reducing antioxidant power assay	India	71
			Toxicological:	The formulation exhibited dose dependent inhibitory activity in the two tested cell lines. It exhibited dose-dependent toxicity (66.57% inhibition) against fibroblasts cells at the highest dose (320 µg/mL). Also, it exhibited higher inhibitory activity (61.88%) against human malignant melanoma A375 cell line.	*In vitro* cytotoxicity test using normal fibroblast cell line NIH3T3 and human malignant melanoma cell line A375		
63.	PHF5	*Peganum harmala, Saussurea lappa, Boswellia carterii, Commiphora myrrha,* and *Artemisia judaica*	Anti-oxidant:	PHF5 showed a dose-dependent antioxidant activity. At the concentrations of 5, 10, and 20µg/mL, the percentage scavenging activity was 35%, 45%, and 70%, respectively. However, it had low activity when compared with that of ascorbic acid which was 66%, 71%, and 74.5% at concentrations of 5, 10, and 20 µg/mL respectively.	2,2-diphenyl-1-picryl-hydrazyl-hydrate based assay	Saudi Arabia	73
			Toxicological:	The result showed that all the mice that received a single dose of PHF5 (2,000 mg/kg body weight) survived the 14-day treatment. No abnormal changes were observed in behavior, tremors, salivation, skin, fur, and eyes. However, histopathological changes were observed in the liver tissues. PHF5 displayed anticancer activities via apoptosis. After 48 h, PHF5 showed a promising inhibitory effect against all cancer cells. The IC_{50} values of PHF5 were 71.8, 64.8, 45.3, and 47.3 µg/mL against LoVo, HepG2, MCF-7, and MDA-MB 231 cells, respectively. The PHF5 extract reduced the viability of all cell lines in a dose dependent manner.	*In vivo* assay using female albino mice and Human cancer cells (MCF-7, MDA-MB 231, LoVo, and HepG2) using the MTT assay		
64.	Evans healthy bitter, Yoyo bitter, Fidson bitter, Swedish bitter, Oroki herbal mixture, Pax herbal mixture, Asheitu Adams blood purifier (ABP), and Asheitu Adams formula for diabetes (AD)	-	Toxicological:	The result revealed that Fidson bitters and Asheitu Adams blood purifier significantly decreased superoxide oxidase and glutathione-S-transferase, while Yoyo bitter and Asheitu Adams formula mostly decreased reduced glutathione in a non-significant manner. In addition, the polyherbal medicines caused decrease in the hepatic concentrations of GST, SOD and CAT levels of the experimental animals.	Enzymatic and *in vivo* antioxidants in albino rats	Nigeria	14

			Anti-oxidant:	The result showed that Irochel possesses strong antioxidant activity. At a concentration of 0.5 mg, Irochel extract showed 85.7% significant radical scavenging activity while gallic acid showed 98.1%.	The extract (Irochel) was analyzed for free radical scavenging activity by 2, 2- diphenyl-1-picrylhydrazyl (DPPH)		
65.	Irochel	*Fagonia cretica (whole plant), Triticum aestivum (wheatgrass), Emblica officinalis (fruit pulp), Cucurbita pepo (seed), Momordica charantia (fruit pulp), and Tribulus terristris (fruit).*	Toxicological:	The result showed a progressive increase in mortality of brine shrimp with an increase in the concentration of the solution. At a concentration of 10 µg/mL, the test drug showed low mortality of 16.66% while at 1000 µg/mL it had a mortality of 86.66%. In the acute toxicity study, at the dose of 5000 mg/kg, no treatment related toxic manifestations, behavioral changes, or mortality was observed. In the sub-acute study, no sign of toxicity and lethality was observed, however, there was some hematological and biochemical variations observed at 3 different doses of 2000, 300, and 50 mg/kg bw.	Brine Shrimp and *In vivo* assay using Wistar Rats	Pakistan	112
66.	BSVT	Leaves of *Boerhavia diffusa*, *Solidago virgaurea*, *Vitex negundo,* and thymoquinone	Anti-oxidant:	The study evaluated the antioxidant activity of BSVT in CCl_4 induced hepatorenal toxicity in rats. The results showed that BSVT at a dose of 100 mg/kg was able to recover the reduced levels of superoxide dismutase (SOD) and glutathione peroxidase (GPx), as well as the increased levels of malondialdehyde (MDA), in both liver and kidney tissues in a dose-dependent manner. The results were similar to those of the standard drug Cystone®. The study concludes that BSVT ameliorates the hepatorenal toxicity in a dose-dependent manner.	*In vivo* (rats).	Saudi Arabia	113
67.	DRHM®	*Cymbopogon citratus* (Leaf), *Carica papaya* (Leaf), *Mangifera indica* (Bark), *Moringa oleifera* (Leaf), *Citrus limon, Psidium guajava, Zingiber officinale* and *Allium sativum*	Anti-oxidant:	The results show that DRHM® has significant antioxidant activity in treating hydrogen peroxide-induced oxidative stress in rats. The study found that H_2O_2 intoxication significantly decreased serum activities of SOD, CAT, and GPx, while DRHM® treatment significantly increased the activities of these enzymes. In addition, DRHM® treatment significantly decreased the MDA concentration and increased the GSH concentration compared to the H_2O_2 control. The findings suggest that the phytoconstituents in DRHM® are responsible for the ameliorative effects of boosting the antioxidant defense system.	*In vivo* (rats).	Nigeria	114
			Toxicological:	The polyherbal formulation was tolerable up to 10 mL/kg b.w since there was no significant behavioural and body weight change as well as mortality within the study period. This finding indicates that the lethal dose is higher than 10 mL/kg b.w. The polyherbal formulation was tolerable in mice up to 10 mL/kg b.w, showing that the lethal dose is above 10 mL/kg b.w and hence, DRHM® is relatively safe. However, further studies are warranted to evaluate the long-term effects of using this polyherbal formulation especially at the molecular level.	*In vivo* assay using male Swiss albino mice		

68.	Livshis	*Berberis aristata* (Stem bark), *Phylanthus niruri* (Leaf), *Andrographis paniculata* (Leaf), *Aloe indica* (Leaf), *Picrorhiza kurroa* (Rhizome), *Asteracantha longifolia* (Leaf), and *Fumaria parviflora* (Leaf)	Anti-oxidant:	The results indicated that CCl4-induced liver damage significantly decreased the activities of hepatic antioxidant enzymes such as catalase (CAT), peroxidase (Px), glutathione-S-transferase (GST), and superoxide dismutase (SOD), as well as the level of vitamin C, while elevating the lipid peroxidation level. However, the administration of "Livshis" resulted in a significant recovery in the levels of these biosensors toward the control level. In comparison, the distilled water-pretreated cum CCl_4-injected animals did not recover significantly from the liver damage induced by CCl_4.	*In vivo* study using male albino rats	India	115
			Toxicological:	The study depicted that treatment with Livshis up to 3200 mg/kg did not produce any lethal or toxic symptoms in the rats. During the 14-day period after the oral administration, no mortality or morbidity, no tremors, salivation, diarrhoea, sleep, coma, death, or unusual behaviours were observed in the rats.	*In vivo* study on male albino rats		
69.	Livomap	*Boerhavia diffusa,Melia azadirachta, Trichosanthes cucumerina, Zingiber officinale, Picrorhiza kurroa,Tinospora cordifolia, Cedrus deodara, Terminalia chebula, Crataeva religiose, Moringa oleifera, Berberis aristate, Artemisia absinthium, Tephrosia purpurea, Phyllanthus niruri*	Anti-inflammatory:	The results showed that administration of ethanol to rats increased the levels of lipid peroxidation products such as thiobarbituric acid reactive substances (TBARS) and hydroperoxides (HP) and decreased the levels of antioxidants. Co-administration of Livomap with ethanol significantly reduced the levels of these lipid peroxidative products and increased the levels of non-enzymatic antioxidants such as vitamin C, vitamin E and reduced glutathione to near normal as compared to ethanol-induced rats. Livomap was found to be beneficial in alleviating ethanol-induced oxidative damage. The study suggests that Livomap could reduce the generation of free radicals and increase the scavenging mechanism of free radicals. The results also showed that Livomap significantly increased the activities of antioxidant enzymes such as SOD, CAT and GPx, which are important components of the cellular defense system against ROS and RNS, and are defense against oxidative damage by supplying NADPH, which is needed for the regeneration of GSH	*In vivo* model on albino wistar rats	India	16

70.	GOV	*Gongronema latifolia* (Leaf), *Ocimum gratissimum* (Leaf) *and Vernonia amygdalina* (Leaf)	Anti-oxidant:	The results showed that GOV possessed significant antioxidant activity. It dose-dependently increased the activity of CAT, GPx, GSH, GST, SOD, and total protein in the serum, kidney, and liver of the rats with acetaminophen (APAP)-induced damage compared to the toxin control groups. Also, GOV significantly reduced the Malondialdehyde (MDA) contents in the liver of rats compared to the toxin-induced control group. The serum levels of CAT, GPx, GSH, GST, and SOD were significantly decreased in the APAP-treated toxin control group compared to the groups that were administered different doses (2, 4, and 8 g/kg) of GOV. However, the activities of these enzymes were restored to normal by GOV administration. At 8 g/kg, GOV significantly increased the activity of GSH compared to all the groups, while at 4 g/kg, GOV increased the levels of GSH, GST, and total protein compared to Liv 52 and Silymarin groups.	*In vivo* study using Wistar albino rats	Nigeria	116
			Toxicological:	The study depicted that the oral (16,000 mg/kg) and intraperitoneal (2,500 mg/kg) administration of GOV did not result in deleterious effect or mortality 24 hr after and within seven days post treatment irrespective of the extract doses tested.	*In vivo* study using Wistar albino rats		
71.	Livomyn	*Andrographis paniculata, Phyllanthus niruri, Triphala, Boerhaavia diffusa, Amoora rohituka, Chicorium intybus, Adhatoda vasica, Eclipta alba, Zingiber officinale, Berberis aristata, Fumaria officinalis, Embellia ribes, Tephrosia purpurea, Tinospora cordifolia, Coriandrum sativum, Aloe barbadensis, Picrorrhiza kurroa.*	Anti-oxidant	The IC_{50} value of the formulation was found to be 62.45, indicating that Livomyn has significant antioxidant activity. Its antioxidant activity was also compared to ascorbic acid (ASC) as a standard, and the results showed that Livomyn was effective in action on free radicals. The results showed that the polyherbal formulation has the potential to scavenge free radicals, which are known to be the main cause of oxidative damage.	*In vitro* by 1, 1-diphenyl-2-picrylhydrazyl (DPPH) assay	India	117
72.	Habb-e-Asgand	*Ptychotis ajowan* (Fruit), *Withania somnifera* (Root), *Gmelina asiatica* (Stem), *Curculigo orchiodes* (Root), *Piper longum* (Fruit and Root), *Asparagus racemosus* (Root), *Zingiber officinale* (Rhizome), *Saccharum officinarum* (Stem)	Anti-oxidant:	The study found that paracetamol induced oxidative stress in the liver of mice, as well as a decrease in the activity of antioxidant enzymes such as glutathione reductase (GR), glutathione peroxidase (GPx), glutathione S-tranferase (GST), catalase (CAT), and glutathione (GSH) contents. However, Habb-e-Asgand (250 mg/kg) showed significant antioxidative potential against paracetamol toxicity. It increases the activity of GR, GPx, GST, and CAT. These findings suggest that the antioxidant constituents in Habb-e-Asgand may be mediating the attenuation of liver injury caused by paracetamol metabolites. The study concludes that Habb-e-Asgand may be used as a prophylaxis for ROS related liver injury.	*In vivo* assay using Swiss albino male mice	India	61

73.	Heptoplus	*Phyllanthus amarus* (Whole plant), *Eclipta alba* (Leaf), *Tephrosia purpurea* (Leaf), *Curcuma longa* (Rhizome), *Picrrohiza kurooa* (Root), *Withania somnifera* (Root), *Pinius succinifera* (Amber), *Pistacia lentiscus* (Resinous exudates), *Orchis mascula* (Seed) and *Cycas circinalis* (Flower)	Anti-oxidant:	The findings showed that rats treated with isoniazid and rifampicin experienced severe oxidative stress by free radicals induced lipid peroxidation. This led to an abnormal index of serum biochemical markers for liver function and increased liver lysosomal enzymes activity. However, rats nourished with 100 mg/kg of heptoplus and Liv 52 were protected from oxidative damage by maintaining a normal antioxidant profile status and restored normal serum liver biochemical markers. Additionally, increased liver lysosomal enzymes activity was prevented in the rats supplemented with heptoplus and Liv 52. The study also revealed that MDA formation, a marker of oxidative insult, was significantly reduced in rats treated with heptoplus and Liv 52.	*In vivo* assay using Sprague Dawley rats	India	62
74.	Livergen	*Andrographis paniculata, Apium graveolens, Berberis lycium, Carum copticum, Cichorium intybus, Cyperus rotundus, Eclipta alba, Ipomoea turpethum, Oldenlandia corymbosa, Picrrorhiza kurroa, Plumbago zeylanica, Solanum nigrum, Tephrosia purpurea, Terminalia arjuna, Terminalia chebula, Trigonella foenumgraecum*	Anti-oxidant:	Livergen exhibited significant antioxidant activity, as determined by its ability to scavenge the DPPH radical. The IC_{50} value of the formulation was found to be 62.45, which was comparable to that of ascorbic acid. The phenolic and flavonoid compounds present in the herbal extracts may have contributed to the antioxidant activity of the polyherbal formulation. The antioxidant activity of Livergen suggests its potential use in protecting against oxidative stress-related diseases.	*In vtro* study using DPPH	India	63
75.	Punarnavashtak kwath (PNK)	*Boerhaavia diffusa* (Root), *Picrorhiza kurroa* (Root), *Tinospora cordifolia* (Stem), *Zingiber officinalis* (Rhizome), *Berberis aristate* (Stem), *Terminalia chebula* (Fruit), *Azadirachta indica* (Bark), and *Tricosanthes dioica* (Leaf)	Anti-oxidant:	The results demonstrated that PNK (100 and 500 mg/kg) has significant antioxidant activity as it significantly increased the levels of glutathione, superoxide dismutase, and catalase compared to the CCl_4-treated group. Additionally, the decreased level of TBARS indicates that PNK has an anti-lipid peroxidative and/or adaptive nature against the damaging effects of free radicals produced by carbon tetrachloride.	*In vivo* (Wistar rats)	India	64
			Toxicological:	The acute toxicity result showed that there was no mortality at any of the tested doses (up to 3000 mg/kg) at the end of 14 days.	*In vivo* (Wistar rats)		
76.	Karisalai Karpam tablet	*Eclipta prostrata, Wedelia calendulaceae, Indigofera tinctoria, Sphaeranthus indicus, Centella asiatica, Acalypha indica, Coldenia procumbens*	Anti-oxidant:	The study found that treatment with Karisalai Karpam resulted in a significant increase in the levels of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and non-enzymatic antioxidant glutathione (GSH) in the liver tissue of rats. In particular, Karisalai Karpam at 100 and 200 mg/kg doses significantly produced *in vivo* antioxidant activity by restoring liver GSH, blood GSH, SOD, CAT, and GPx levels. Karisalai Karpam (200mg/kg) was found to be effective in increasing liver and blood GSH, SOD, and CAT levels.	*In vivo* using Wistar rats	India	66
77.	Aab-e-Murawaqain	*Solanum nigrum* and *Cichorium intybus*	Anti-oxidant:	The results showed that CCl4 administration caused a significant increase in TBARS levels and a decrease in GSH, SOD, and CAT levels in hepatic tissues. However, treatment with the polyherbal formulation (4.5 ml/kg) significantly reduced TBARS levels and increased GSH, SOD, and CAT levels, indicating its antioxidant potential.	*In vivo* (Wistar albino rats)	India	118

78.	Virgoliv syrup (VLS)	*Eclipta alba* (Whole plant), *Plumbago zeylanica* (Root), *Andrographis paniculate* (Whole plant), *Boerhavia diffusa* (Root), *Solanum nigrum* (Whole plant), *Tecomella undulate* (Stem bark), *Picrorhiza kurroa* (Rhizome), *Cissampelos pareira* (Root), *Operculina turpethum* (Root), *Embelia ribes* (Fruit), *Cichorium intybus* (Seed), *Phyllanthus niruri* (Whole plant), *Tinospora cordifolia (Stem), Tephrosia purpurea* (Whole plant), *Piper longum* (Fruit), *Berberis aristate* (Stem), *Cassia occidentalis* (Seed)	Anti-oxidant:	The study depicted that Virgoliv syrup (1 ml/kg) showed significant antioxidant activity against CCl_4-induced hepatic damage as the levels of antioxidant enzymes such as CAT, GSH, and SOD were significantly increased in liver tissue of rats treated with Virgoliv syrup and silymarin when compared to CCl_4-treated rats. The increased MDA levels observed in CCl4-treated rats were also reduced after treatment with Virgoliv syrup.	*In vivo* assay using Sprague-Dawley rats	India	68
			Toxicological:	The result of acute toxicity study revealed that VLS was safe up to 2000 mg/kg. The rats were alive, active and healthy during the period of observation.	*In vivo* assay using Sprague-Dawley rats		
79.	BV-7310	*Phyllanthus niruri, Tephrosia purpurea, Boerhavia diffusa,* and *Andrographis paniculata*	Anti-oxidant:	BV-7310 demonstrated potent antioxidant activity, as evidenced by its lower IC_{50} value of 20 µg/ml compared to individual extracts of *A. paniculata, B. diffusa, P. niruri, and T. pupurea.* The results suggest that the combination of these plant extracts in BV-7310 has a synergistic effect on antioxidant activity.	*In vitro* model using DPPH	India	67
80.	HP-4	*Aloe vera* (Leaf), *Bacopa monnieri* (Leaf), *Moringa oleifera* (Leaf) and *Zingiber officinale* (rhizome)	Anti-oxidant:	The polyherbal formulation HP-4 (100mg) showed significant antioxidant activity, as evidenced by increasing the levels of SOD, GPx, GR, and GSH, while decreasing the levels of TBARS in the liver homogenates of mice. These findings suggest that HP-4 has the potential to prevent oxidative stress-induced liver damage caused by free radicals.	*In vivo* (mice)	India	65
81.	Livplus-A	*Eclipta alba* (Whole plant), *Phyllanthus niruri* (Whole plant), *Cichorium intybus* (Whole plant), *Picrorhiza kurroa* (Root), *Boerhaavia diffusa* (Whole plant), *Berberis aristata* (Whole plant), *Andrographis paniculata* (Whole plant)	Anti-oxidant:	The study showed that the levels of endogenous anti-peroxidative enzymes such as SOD and catalase were increased, and the glutathione contents were increased in rats treated with Livplus, indicating its antioxidant activity. Therefore, it can be inferred that Livplus may have a significant impact on reducing oxidative stress in the liver, making it an effective antioxidant	*In vivo* Albino Wistar rats	India	119
			Toxicological:	The oral administration of Livplus in rats up to the dose 2000 mg/kg did not show any sign of toxicity and no mortality for 14 days, indicating that Livplus up to oral dose of 2000 mg/kg of body weight is safe.	*In vivo* Albino Wistar rats		
82.	Ambrex	*Withania somnifera, amber*, *Pistacia lentiscus*, *Orchis mascula* and *Cycas circinalis*	Anti-oxidant:	The result revealed that Ambrex (250 and 500 mg/kg) and showed significant antioxidant activity as it was able to restore the levels of SOD, catalase, and glutathione, to near-normal levels. The study also showed that Ambrex inhibited the formation of hepatic malondialdehyde induced by MTX. These findings suggest that Ambrex may protect the liver against oxidative stress-induced damage, possibly by enhancing the levels of endogenous antioxidants and inhibiting the expression of pro-apoptotic genes	*In vivo* assay using Swiss albino mice.	India	120

83.	Polyherbal formulation (CFCT)	*Costus speciosus, Fumaria indica,* and *Cichorium intybus*	Anti-oxidant:	The study found that cisplatin-induced hepatorenal toxicity resulted in a significant increase in oxidative stress markers such as MDA levels and a decrease in antioxidant parameters such as SOD, GPx, GST, and CAT activities. However, the administration of the CFCT formulation significantly restored the levels of these antioxidant parameters, which could be attributed to the formulation's contribution to the antioxidant defense system by scavenging free radicals and reducing oxidative stress and inflammatory responses	*In vivo* study using male Wistar rats	Saudi Arabia	121
84.	Zereshk-e-Saghir (ZES)	*Berberis vulgaris, Rosa damascene, Cichorium intybus, Cucumis sativus, Portulaca oleracea, Rheum palmatum,* and *Nardostachys jatamansi*	Anti-oxidant:	The polyherbal formulation decreased lipid peroxidation and maintained the levels of glutathione and total antioxidant capacity. These findings suggest that ZES has a significant antioxidant effect, which protects against liver damage. Compared to the control group, the study found that the polyherbal formulation had a better antioxidant effect on the liver.	*In vivo* assay in a rat model	Iran	122
			Toxicological:	The acute toxicity result showed that there was no mortality or morbidity observed in the rats after the oral administration of single doses of 1000 and 2000 mg/kg.	*In vivo* assay in a rat model		
85.	Polyherbal formulation (PHF)	*Cajanus cajan, Lawsonia inermis Mimosa pudica, Uraria picta* and *Operculina turpethum*	Anti-oxidant:	The results demonstrated that PHF prevents the depletion level of GSH and decrease in the activity of SOD in CCl4-induced liver injury in rats. In addition, PHF also showed a significant decrease in the LPO levels signifying the potent antioxidant activity.	*In vivo* using albino rats.	India	123
			Toxicological:	In the acute toxicity study, the doses of 1000, 2000 and 4000 mg/kg showed no mortality or any behavioral changes in the rats.Thus, the PHF was considered to be safe up to 4000 mg/kg.	*In vivo* using albino rats.		
86.	Tritone (Livosone)	*Eclipta alba, Tinospora cardifolia, Curcuma longa* and *Picrorrhiza kurroa*	Anti-oxidant:	The results showed that Tritone (Livosone) had free radical scavenging activity comparable to that of the standard antioxidant ascorbic acid. In addition, the study found that as the concentration of Tritone increased, the free radical scavenging activity also increased.	*In vitro* assay using DPPH	India	124
87.	Polyherbal capsule	*Andrographis paniculata* (Whole plant), *Phyllanthus amarus* (Whole plant), *Asparagus racemosus* (Root), *Tinospora cordifolia* (Stem), *Boerhaavia diffusa* (Root) and *Eclipta alba* (Whole plant)	Toxicological:	The result showed that no mortality was observed at 2000mg/kg dose.	*In vivo* method using Adult male Albino Wistar rats	1ndia	125
88.	PHF used for the treatment of dental plague	*Azadirachta indica* (leaves), *Terminalia chebula* (whole fruit), *Terminalia belerica* (whole fruit), *Emblica officinales* (dried pulp of fruit), *Terminalia arjuna* (bark) and *Mangifera indica* (leaves).	Anti-oxidant:	The oral toxicity result showed the extract to be safe for use.	I*n vivo* assay using Sprague Dawley rats	India	126

89.	Daouri	*Khaya senegalensis, Odina acida, Lophira lanceolata, Paullinia pinnata* and *Pteleopsis suberosa etc.*	Toxicological:	The result showed that after 28 days administration of Daouri (300-1200 mg/kg), the body weight of the rats was not affected. However, compared with the control group, low body variation was observed. The serum concentration of alanine transaminases, creatinine and urea were not affected, but the serum concentration of alkaline phosphatase was increased. In addition, abnormality was observed in the livers of the rats.	*In vivo* assay using Wistar rats	Togo	79
90.	PHF used in the treatment for various ailments such as malaria, typhoid, waist pain, back pain	*Hibiscus sabdariffa* and *Aloe barbadensis*	Toxicological:	No notable behavioral changes or mortality was observed in rats during the acute toxicity testing. The sub chronic administration remedy did not cause any significant changes in the serum activities of liver-function enzymes, hematological markers, serum electrolytes and other evaluated blood-chemistry indices. The liver photomicrographs showed that treatment of animals with the polyherbal mixture did not induce any visible lesions or derangements in the examined organ.	*In vivo* assay using Wistar rats	Nigeria	82
91.	Tabsaab used for the cure of tuberculosis	*sesamum indicatum, Vernonia amygdalina, Aloe barbadensis, Saccharum officinarum, Allium sativum* and *Amaranthus caudatus*. The parts used were not mentioned	Toxicological:	For the 8-week monitoring period, the study showed a 100% recovery rate in females and a 98% recovery rate in males, with no toxicity or side effects observed in the patients.	*In vivo* experiment using human	Nigeria	76
92.	Hab-e-Kabad Noshadri tablets used for the treatment of hepatitis, enlargement of liver, liver function disorders, dyspepsia, flatulence, abdominal pain, nausea, vomiting, lack of appetite, constipation and carminative.	Ammonium chloride, Black, lake and common salts, *Curcuma zedoaria, Sodium borate Zingiber officinale, Terminalia chebula, Embelia ribs, Rosa indica, Terminalia belerica, Piper nigrum, Cassia angustifolia, Cassia acutifolia* and *Terminalia chebula.*	Toxicological:	In the acute toxicity study, no morbidity and mortality were observed with single dose administration 2000 mg/kg/day BW) in the mice. In the sub-acute toxicity study, no significant changes with 50 mg/kg/day, but at doses of 100 and and 200 mg/kg/day, morphological changes with some damage in liver and kidney tissues of male and female animals was observed. Hence, prolonged use at higher dose i.e. 200 mg/kg/day of this polyherbal formulation should be avoided.	*In vivo* assay using Swiss mice and Albino Wistar rats	Pakistan	85
93.	Herbal formulation used for gynecological disorders	*Saraca indica*, *Symplocos racemosa*, *Valeriana wallichii*, *Matricaria chamomilla*, *Vitex agnuscastus* and *Areca catechu*.	Toxicological:	The result of acute toxicity after oral administration reveals that the herbal formulation has LD_{50} greater than 5000 mg/kg In the sub-chronic toxicity, no significant changes in biochemical, hematological and histopathological parameters was observed. However, some indicators such as urea, creatinine, hemoglobin, and RBC count were altered.	In vivo assay using Albino mice and white rabbits	Pakistan	80
94.	Yagari used for the management and treatment of prostate disorder	*Nauclea latifolia,* and *Erythrophleum suaveolens.*	Toxicological:	In the acute assay, no mortality or uncoordinated movement was observed in the rats treated with doses up to 5000 mg/kg body weight. The sub-chronic toxicity revealed that at concentrations of 250, 500 and 1000 mg/kg, no significant changes in the hematological and histopathological parameters was observed, however, the body weight of the rats significantly increased.	Acute oral toxicity was carried out in Swiss mice while sub-chronic toxicity study was carried out with adult Albino rats	Nigeria	83
95.	Ade & Ade Antidiabetic®" used in the treatment of diabetes	*Ocimum gratissimum* (leaves), *Citrullus lanatus* (leaves), *Momordica charantia* (leaves), *Chrysophyllum delevoyi* (leaves), and *Uncaria tomentosa* (leaves).	Toxicological:	There were no noticeable changes in the nervous system responses or adverse gastrointestinal effects observed in the male and female mice used during the experimental period in the acute toxicity study.	*In vivo* assay using Swiss mice and Albino Wistar rats.	Nigeria	78

96.	Hb cleanser® bitters	*Aloe vera, Acinos arvensis, Moringa oleifera, Allium sativum, Chenopodium murale* and *Cinnamomum aromaticum.*	Toxicological:	Acute toxicity results showed that the LD_{50} of HB Cleanser Bitters was greater than 5000 mg/kg with no mortality. There was a significant increase in body weight. In addition, at 1 ml/kg, there was significant increase in total bilirubin, conjugated bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and urea more than the other doses compared to negative control. A significant decrease was observed in the levels of total protein and albumin compared to negative control. Hence. HB cleanser Bitters may adversely affect hepatic and renal indices and therefore should be used with caution.	*In vivo* assay using adult Wistar rats	Nigeria	87
97.	Orijin Bitters, Baby Oku, Kummerling Herbal liqueur, 1960 Alcoholic Bitters, Adonko Alcoholic Bitters, Action Bitters, Alomo Bitters, Bajinotu Poka Alcoholic drink, Aleko, Okiki Ibile, Opa Eyin, Ewe Dongoyaro, Jedi and Awopa	-	Toxicological:	The pathological examination of the animals showed that the heart of the group treated with Jedi had chronic inflammatory cell infiltrates, while the hearts of the other groups showed no abnormalities. The kidney tissue showed congested vessels and the lung tissue showed a reduction in air-filled alveolar spaces and infiltration of alveoli and interstitium by aggregates of inflammatory cells, indicating moderate to severe pulmonary inflammation. The lung tissue of rats treated with herbal liquors showed congestion of pulmonary vessels and interstitial hemorrhages. The genotoxic evaluation of rat lymphocytes showed that the rats administered with the herbal liquors developed significant DNA strand breaks, indicating oxidative DNA damage. These results suggest that the herbal liquors contain substances that produce reactive oxygen species that have pathological effects on certain organs and can lead to DNA damage and mutations.	*In vivo* assay using Wistar rats	Nigeria	127
98.	Drepanoalpha® hard capsules used for the management of sickle cell disease	*Justicia secunda* (leaves) and *Moringa oleifera* (leaves)	Toxicological:	In the acute toxicity test, no mortality occurred at the limit dose of 5000 mg/kg of B.W. during the observation period of 14 days. However, slight changes in behavior, respiration and hypoactivity were observed in treated Guinea pigs for a few minutes after dosing. No sign of toxicity or organ damage was observed on the tested organs (heart, stomach, kidneys, liver). The results of haematological (red and white blood cells counts, haemoglobin, haematocrit) and biochemical (ALT, AST, albumin, total protein) tests did not show significant differences between control and test groups.	*In vivo* experiment using Guinea pigs	Congo	84
99.	Ade & Ade used for systemic detoxifiers and as diuretic agent	-	Toxicological:	At the different doses administered in the acute toxicity study, no mortality, no changes in their feeding habits, stool, urine and the animals were active throughout the study. In the sub-chronic toxicity study, the formulation reduced cholesterol level at low and high doses in animals, it may be beneficial on cardiovascular risk factor. In addition, the formulation had no side effect on the liver, heart and the kidney in all the doses.	*In vivo* assay using Swiss mice and Albino Wistar rats.	Nigeria	81

100.	Bobwell® used for the management of diabetes mellitus.	*Gongronema latifolium* (leaves), *Garcinia kola* (leaves), *Vernonia amgydalina* (leaves), *Sphenocentrum jollyanum* (leaves) and *Kigelia africana* (leaves)	Toxicological:	In the acute toxicity study, no changes in the behavior, no adverse gastrointestinal effects and no changes in the sensory nervous system responses were observed in the animals. In the animals that received the highest dose, there was significant increase in their body weight, alanine aminotransferase (ALT), decrease in the plasma glucose level, and increase in creatinine level while aspartate aminotransferase (AST) decreased significantly. The photomicrograph of hepatic tissue showed focal necro-inflammation around the portal hepatics. There was marked increase in the haemoglobin level and in the red blood cell count and white blood cells.	*In vivo* assay using Swiss albino mice	Nigeria	128
101.	YoyoBitters™, Ogidiga™ and BabyOku™)	-	Toxicological:	The result showed a dose dependent decrease in the hemoglobin concentration and percentage packed cell volume; red blood cell, white blood cell, lymphocytes, neutrophil and platelets counts (2 mL/kg bwt). Also, a dose- and tissue-dependent increase in induction of apoptotic DNA fragmentation was observed in the triherbal groups relative to control groups. Also, an increase in micronucleated polychromatic erythrocytes was formed in a dose-dependent manner in the multi-herbal groups when compared with the control groups.	*In vivo* assay using Wistar rats	Nigeria	129
102.	OsomoBitters™ Ogidiga™ and BabyOku™	*Callichilai barteri, Pachylobus Edulis, L. cupanioides, Allium sativum, Zingiber officinale, Monodora myristica, Khaya ivorensis, Piper nigrum.* Eugenia caryophyllus ethanol, water, sugar, lemon, garlic, ginger and combretaceae. Carene, eugenol, propenoic acid and nonanoic acid and cyclohexanemethanol, water, ethanol, caramel, angelia root, *cassia sanna* (sic) leaf, rhuherb root and aloe	Toxicological:	The remedies showed a dose- and tissue-dependent increase in induction of apoptotic DNA fragmentation in the polyherbal groups relative to control groups. Also, an increase in micronucleated polychromatic erythrocytes were formed in a dose-dependent manner in the polyherbal groups when compared with the control groups. The haematological parameters showed dose dependent decrease in the hemoglobin concentration and percentage packed cell volume; red blood cell, white blood cell, lymphocytes, neutrophil and platelets counts	*In vivo* assay using Wistar rats	Nigeria	130
103.	Hydroalcoholic polyherbal formulation (HAF)	*Bergenia ciliate* (root), *Pedalium murex* (fruits), *Tribulus terrestris* (fruit), *Sphaeranthus indicus* (flower), *Tinospora cordifolia* (stem), *Piper longum* (fruit)	Toxicological:	No abnormality and sign of toxicity produced at a dose of 2000 mg/kg body weight. The HAF was found to be safe up to a dose of 2000 mg/kg body weight.	*In vivo* assay using Sprague Dawley female rats	India	131

highlights the importance of thoroughly researching and evaluating the effectiveness of polyherbal remedies before using them to treat infections.

Interestingly, Triple bark and some formulations showed antibacterial activity that was significantly higher than the control drugs,[40,41] while NOQ19 showed excellent antiviral efficacy, eliminating 100% of the virus at a concentration of 0.9 mg/mL, with an IC_{50} of 0.2 mg/mL.[24] These findings suggest that certain polyherbal formulations have the potential to be used as effective treatments for bacterial, fungal, and viral infections. Additionally, the study found that some of the polyherbal remedies exhibited anti-tubercular activity, with the most active remedies being KWTa, HBfs, and HBts, which exhibited inhibitory activity against *M. tuberculosis* at 1.562 µg/mL.[39] This highlights the potential of polyherbal remedies as an alternative or complementary treatment for tuberculosis, which is a major global health concern. According to Famewo *et al.*[42] some of these polyherbal formulations contain the essential mineral nutrients and vitamins that could probably be boosting the immune system of tuberculosis patients. Thus, they can enhance the immune system and help the host fight against microbial infections by increasing the activity of immune cells, such as macrophages, neutrophils, and natural killer cells.

The differences observed in the MIC values of the reviewed polyherbal formulations against various microorganisms could be attributed to several factors, including the mode of action of the formulations by direct inhibition of the growth and proliferation of microorganisms or disruption of microbial cell membranes, the differences in cell wall composition and/or genetic makeup of the microorganisms as well as the synergistic effects of different phytoconstituents present in the herbal formulations. These findings are important as they highlight the potential benefits of using polyherbal formulations. However, further research is needed to determine the effectiveness of these remedies on a larger scale and against a wider range of microorganisms. Additionally, studies should be conducted to determine the safety and potential side effects of these formulations before they can be recommended for widespread use. Overall, this review provides valuable insight into the potential of polyherbal remedies as a natural and effective means of treating bacterial infections.

Anti-inflammatory activity of polyherbal formulations

Inflammation management often involves non-steroidal anti-inflammatory drugs (NSAIDs), which inhibit the activity of the cyclooxygenase-2 (COX-2) enzyme, preventing the synthesis of prostaglandins like prostaglandin E-2.[9] However, among other effects, the use of NSAIDs can result in dependence, prove to be financially unfeasible and challenging to access, and may result in adverse effects such as nephrotoxicity, cardiotoxicity, hepatotoxicity, intestinal bleeding, and gastric ulcers.[43-45] The upregulated synthesis of inflammatory mediators results from the activation and enhanced activity of inducible nitric oxide synthase (iNOS), COX-2 enzymes, and pyrogenic cytokines such as tumour necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interleukin (IL-6), among others.[9,46] Therefore, to qualify as an anti-inflammatory agent in an *in vivo* assay, it should alter the effects of carrageenan-induced inflammation, leading to the alleviation of typical features such as redness, oedema, pyrexia, algesia, and tissue dysfunction.[46,47]

The results of the studies indicate that the polyherbal medicines investigated possess anti-inflammatory activities, with some of these remedies used in wound and diabetes management. Phytexponent, a polyherbal medicine used for pain and inflammation treatment, was examined for its anti-inflammatory activity using carrageenan-induced paw oedema mice. The study found that Phytexponent demonstrated significant anti-inflammatory effects in a time-dependent manner, with greater efficacy at 250 mg/Kg BW than the positive control indomethacin (4 mg/Kg BW). The polyherbal medicine also significantly reduced oedema in a dose- and time-dependent manner, and it effectively inhibited both the early and late phases of inflammation. The study suggests that Phytexponent's anti-inflammatory effects could be attributed to the inhibition of the COX enzyme. The time-dependent increase in percentage inhibition of oedema may be due to a higher bioavailability of active molecules, following metabolism and distribution to target sites.[9] Overall, these findings suggest that polyherbal medicines such as Phytexponent could be considered potential alternatives for the management of inflammation, as they demonstrate promising anti-inflammatory effects. Further studies are necessary to explore the mechanisms of action of this remedy.

In addition, IBS-20 used for the treatment of irritable bowel syndrome, showed potent anti-inflammatory effects on innate immune cells *in vitro* as well as on the murine model of colitis *in vivo,* by suppressing the up-regulation of key inflammatory cytokines.[48] Furthermore, Dev *et al.* reported that PHGs (2% and 5%) used for wound healing showed significant and maximal anti-inflammatory activity after 180 min in carrageenan-induced paw oedema as compared to normal control and negative control animal groups.[3] The inflammation induced by the carrageenan lasts approximately up to 5 h after injection. Also, the AHPL/AYCAP/0413 Capsule used in the treatment of Acne exhibited anti-inflammatory activity with a significant reduction in rat paw oedema (51% inhibition) which was comparable to that of the control, Diclofenac (58% inhibition).[49] The ethanolic extracts of THR-SK010 and THR-SK011 polyherbal inhibited nitric oxide (NO) production, suggesting its potential in the treatment of inflammation and wounds.[50] The findings suggest that polyherbal medicines can be effective in managing inflammation and offer a safer alternative to non-steroidal anti-inflammatory drugs with their known adverse effects.

During inflammation, lysosomal hydrolytic enzymes can be released into the surrounding tissues, causing damage to organelles and leading to a variety of disorders. Researchers such as Chamara *et al.* (2018)[51] have investigated the potential anti-inflammatory effects of polyherbal formulations using erythrocyte membrane stabilization methods. This method helps to determine if the formulations have the ability to stabilize lysosomal membranes and prevent the release of lysosomal components that can cause inflammation and tissue damage. Chamara *et al.*[51] found that both formulations exhibited moderate anti-inflammatory activities, which could be attributed to the phytoconstituents of the herbal formulations, which exert intense stabilizing effects on lysosomal enzymes. Lysosomal stabilization is important in reducing inflammation by preventing the liberation of lysosomal components of activated neutrophils which generally tend to cause tissue damage and inflammation.[52]

Similarly, Abbas *et al.*,[5] investigated the *in vitro* anti-inflammatory activity of different extracts of polyherbal formulations used for treating urinary tract infections using the membrane stabilization method. The findings showed that the water extract (1 mg/mL) exhibit maximum inhibition of inflammation (36.54%), followed by ethyl acetate (33.27%), methanol (25.98%), and hexane (9.44%) extracts. The water, ethyl acetate, and methanol extracts exhibited more effective activity than the standard anti-inflammatory drug Diclofenac sodium (15.42%). It can be deduced that the phytoconstituents present in water extract may stabilize the lysosomal membranes and prevent the release of enzymes that can cause inflammation and tissue damage. Hence, the findings of these studies suggest that polyherbal formulations have the potential to prevent and cure inflammation and tissue damage that may be an emerging effect of various disorders. The stabilizing effects of phytoconstituents present in these formulations on lysosomal enzymes may play a critical role in reducing inflammation and promoting healing.

In conclusion, polyherbal medicines can exert anti-inflammatory effects through various mechanisms of action, depending on the specific herbs and their constitutent bioactive compounds. Polyherbal medicines may help prevent inflammation by inhibiting pro-inflammatory enzymes involved in the production of inflammatory molecules, such as cyclooxygenase (COX) and lipoxygenase (LOX);[53,54] by using antioxidants to scavenge free radicals and reactive oxygen species that are generated during inflammatory processes, thereby reducing oxidative stress and inflammation;[55] by modulating the immune system and reducing inflammation through regulation of the immune cells' (such as macrophages, T cells, and B cells) activities;[56] by stabilization of cell membranes and prevention of the release of pro-inflammatory molecules, such as cytokines and chemokines.[57] Overall, polyherbal medicines can provide a comprehensive approach to preventing inflammation by targeting multiple pathways and molecules involved in the inflammatory response. However, it's important to note that the specific effects and mechanisms of individual herbs may vary, and the safety and efficacy of polyherbal formulations should be evaluated through rigorous scientific studies.

Antioxidant activity of polyherbal formulations

Antioxidants are molecules that can prevent, delay or remove oxidative damage caused by free radicals. They work by reacting with

free radicals, which reduces the harmful effects of oxidative stress.[51] The primary function of antioxidants is to neutralize the excess free radicals and safeguard cells against their toxic effects, thereby helping to prevent diseases.[15] When produced in excess, reactive oxygen species (ROS) can cause oxidative damage by destroying antioxidant enzymes, damaging biological macromolecules such as DNA and RNA, and impairing cell signalling pathways, which can lead to apoptosis or cell death. Different antioxidant compounds can decrease oxidative stress by chelating free radicals, scavenging free radicals, or modulating the activities and levels of antioxidant enzymes and their reducing potential.[18] In addition, phenolic compounds such as phenols, tannins, saponins, flavonoids, and steroids are also known to exhibit antioxidant properties.[58,59] Therefore, phytocompounds are powerful antioxidants that can neutralize and eliminate harmful free radicals.[5]

Free radicals, especially ROS, are involved in carcinogenesis' initiation, promotion, and progression. Oxidative damage to DNA and cellular components caused by ROS can lead to cancer-related mutations.[60] Consequently, antioxidants help in protecting the human body from ROS-induced damage, and consumption of natural antioxidants has been linked to a lower risk of cancer and other diseases associated with oxidative damage, which is linked to phenolic compounds and the phenolic hydroxyl group.[60]

The use of polyherbal formulations for their antioxidant properties has gained attention in recent years due to their potential to protect the human body from free radicals. Various methods, such as DPPH radical scavenging activity, FRAP assay, ABTS radical cation scavenging activity, hydroxyl free radical-scavenging activity, scavenging of superoxide radical, nitric oxide radical scavenging capacity, lipid peroxidation assay, and *in vivo* antioxidants in albino rats, have been used to confirm the antioxidant activity of these polyherbal formulations.

The results have shown that many of the polyherbal formulations exhibited strong antioxidant activities in a concentration-dependent manner, with some showing even more activity than standard drugs. For instance, the polyherbal formulation used for treating urinary tract infections showed the highest scavenging activity of 98.63% which was higher than the natural antioxidant rutin (60.32) and the synthetic BHT (64.40).[5] Similarly, the Thalipathiri Chooranam used for the treatment of cough showed a gradual increase in nitric oxide radical scavenging activity in a concentration-dependent manner, with a maximum reduction of 79.6 (100 µl), which was comparable to the positive control gallic acid (78.9). The reducing power of the remedy was highest at 100 µl (83.29), resulting in the reduction of Fe^{3+} to Fe^{2+} by donating an electron. This indicates that the reduced power capacity of the extract can serve as a significant indicator of its potential antioxidant activity.[35]

The potent antioxidant activity of both THR-SK010 and THR-SK011 against free radicals such as DPPH and hydroxyl radicals may be due to the potent activity of active constituents present in the herbal formulations.[50] The antioxidant capacity of most herbal sources is usually associated with their phenolic contents. Antioxidants that react quickly with free radicals may react slowly or may be inert to the DPPH radical.[5] The higher DPPH radical scavenging activity observed in the polyherbal formulations indicates that the extracts can scavenge other free radicals in the human body. Therefore, natural antioxidant agents have gained attention because they can protect the human body from free radicals.

One study found that Habb-e-Asgand exhibited significant antioxidative potential against paracetamol toxicity by increasing the activity of antioxidant enzymes such as glutathione reductase, glutathione peroxidase, glutathione S-tranferase, catalase, and glutathione contents.[61] Similarly, another study showed that rats treated with isoniazid and rifampicin experienced severe oxidative stress-induced lipid peroxidation, but supplementation with heptoplus and Liv 52 prevented oxidative damage and restored normal serum liver biochemical markers.[62]

In addition, several polyherbal formulations, such as Livergen, PNK, Karisalai Karpam, and HP-4, were found to exhibit significant antioxidant activity by increasing the levels of various antioxidant enzymes and reducing the levels of TBARS, which is a marker of oxidative insult.[63–66] BV-7310, a combination of plant extracts, also demonstrated potent antioxidant activity, suggesting a synergistic effect on antioxidant activity.[67]

Furthermore, the study showed that Virgoliv syrup exhibited significant antioxidant activity against CCl4-induced hepatic damage, as evidenced by the increased levels of antioxidant enzymes such as CAT, GSH, and SOD.[68] These findings suggest that polyherbal formulations have potential therapeutic value in protecting against oxidative stress-related diseases.

However, some PHFs such as Evans healthy bitter, Yoyo bitter, Fidson bitter, Swedish bitter, Oroki herbal mixture, Pax herbal mixture, Asheitu Adams blood purifier, Asheitu Adams formula for diabetes, e.t.c cause depletion of hepatic antioxidant enzymes. The administration of Fidson bitters and Asheitu Adams blood purifier significantly decreased superoxide oxidase and glutathione-S-transferase concentrations in comparison with the control, while Yoyo bitter and Asheitu Adams formula mostly decreased reduced glutathione in a non-significant manner. Additionally, the PHFs caused a decrease in the CAT levels of the experimental animals,[14] which means that the continuous mobilization of these enzymes due to the daily introduction of free radical-generating polyherbal then led to the depletion of antioxidant enzymes as a result of exhaustion in the course of scavenging the overproduced free radicals. Also, the decrease in GSH concentrations, a naturally occurring antioxidant that prevents free radical damage to cells and helps in the detoxification process by conjugating with oxidants, must have resulted from the free radical scavenging activity of GST.[14] It is important to note that while polyherbal formulations have potential benefits, they may also have adverse effects if not used correctly. Therefore, it is necessary to conduct further studies to determine the appropriate dosage and duration of use to ensure maximum benefits and minimal side effects. Additionally, caution should be exercised when selecting and using polyherbal formulations, and it is recommended to consult with a healthcare professional before use.

In conclusion, polyherbal medicines may help prevent oxidative stress by scavenging free radicals and other reactive oxygen species that cause oxidative damage to cells and tissues; by upregulating the expression and activity of endogenous antioxidant enzymes, such as superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT), which help to neutralize free radicals and prevent oxidative damage; by chelation of metal ions, such as iron and copper, which can generate free radicals and promote oxidative stress; and by reducing oxidative stress by suppressing the production of pro-inflammatory molecules, such as cytokines and chemokines.

Toxicological activity of polyherbal formulations

Currently scientists are trying to explore development of new polyherbal therapy. Phytochemcials such as, polyphenols and flavonoids have potent anticancer activities by involving regulation of various signal transduction pathways of cancer cell growth and suppression and proliferation of oncogenes and formation of tumor, modulation of enzyme activity, induction of apoptosis, reduction, oxidation, regulation of hormone metabolism and stimulation of the immune system and DNA repair.[69]

According to the National Cancer Institute (NCI) criteria, plant extracts with CC_{50}< 30 µg/ml are considered to be cytotoxic after 48-72-hour exposure to cells.[70] In the cytotoxicity assay, the therapeutic indexes of the ethanol extract of THR-SK010 were more than 10 (45.68 µg/mL), indicating that the extracts exhibited no cytotoxicity as compared to the positive control ellipticine which had the value of 1.48 µg/mL.[50] Also, phytexponent was found not toxic to Vero E6 cells (CC50 >1000 µg/ml) compared to the control cyclophosphamide (CC_{50}=2.48 µg/mL).[9] The study of Devanathadesikan Seshadri *et al.*[69] revealed that the methanol extract of polyherbal fraction showed cytotoxicity against the two cell lines with the LC_{50} value 467 ± 2.9 mg/ml against HeLa cell line and >800 mg/ml against MCF-7 cell lines. Thus, showing promising anticancer activity against HeLa and MCF cell lines. Phytochemcials such as, polyphenols and flavonoids have potent anticancer activities by involving regulation of various signal transduction pathways of cancer cell growth and suppression and proliferation of oncogenes and formation of tumor, modulation of enzyme activity, induction of apoptosis, reduction, oxidation, regulation of hormone metabolism and stimulation of the immune system and DNA repair. Furthermore, *in vitro* cytotoxicity test of a PHF1 using normal fibroblast cell line NIH3T3 and human malignant melanoma cell line A375 revealed that the formulation exhibited dose dependent inhibitory activity in the two tested cell lines. It exhibited dose-dependent toxicity (66.57% inhibition) against fibroblasts cells at the highest dose (320 µg/mL), and exhibited higher inhibitory activity (61.88%) against human malignant melanoma A375 cell line. Hence, it had cytotoxic effect against melanoma cancer cell line.[71]

In addition, Ramamoorthy *et al.*[41] rated cytotoxicity of the polyherbal formulation on the basis of the percentage viability relative to control group. Samples are considered non-toxic, if the viability is > 90%; the value between 60–90% viability indicates a slight toxicity; 30–59% means a moderate toxicity; and the values < 30% indicates that the sample is severely toxic to the cells.[72] Hence, the result showed that the increasing concentration of the extract decreases the viability of cells and the IC_{50} value of the extract is found to be 274.30 µg/mL. PHF5 displayed anticancer activities *via* apoptosis. After 48 h, PHF5 showed a promising inhibitory effect against all cancer cells. The IC_{50} values of PHF5 were 71.8, 64.8, 45.3, and 47.3 µg/mL against LoVo, HepG2, MCF-7, and MDA-MB 231 cells, respectively. The PHF5 extract reduced the viability of all cell lines in a dose dependent manner and the results confirmed that the inhibition of MCF-7 cell proliferation by the PHF5 extract was capable of inducing apoptosis.[73]

In the acute and sub chronic assays, most of the polyherbal formulations were found to be highly effective at low dose and highly safe even at high dose. For instance, DAS-77® used for the treatment of piles, dysentery, cholera, menstrual pain, stomach disorder, ulcer, constipation, diarrhoea and sexually transmitted infections did not induce lethality in mice when administered orally up to 20 g/kg in divided doses. According to the assertion of Clarke and Clarke,[74] a substance that does not produce lethality up to 10 g/kg orally is relatively non-toxic, hence the herbal preparation can be said to be safe when administered orally. In the study of Singh *et al.*,[75] PHF used for the treatment of dysentery was reported to be safe as no mortality of animals was observed, no significant changes in behavior, postural abnormalities, impairment in food and water intake, and loss or yellowing of hair were also observed in the rats. In addition, Tabsaab used for the cure of tuberculosis was observed for 8-weeks and a 100% recovery rate in females and a 98% recovery rate in males, with no toxicity or side effects was observed in the patients.[76]

The sub chronic administration some remedies did not cause any significant changes in the serum activities of liver-function enzymes, hematological and histopathological parameters, serum electrolytes and other evaluated blood-chemistry indices. The liver photomicrographs showed that treatment of animals with the polyherbal mixtures did not induce any visible lesions or derangements in the examined organ.[77-84]

However, in the sub-acute toxicity study of Hab-e-Kabad Noshadri tablets used for the treatment of hepatitis, enlargement of liver at doses of 100 and and 200 mg/kg/day, morphological changes with some damage in liver and kidney tissues of male and female animals was observed. Hence, prolonged use at higher dose *i.e.* 200 mg/kg/day of this polyherbal formulation should be avoided.[85] Also, decrease in the body weight was observed in rats that received higher doses of Leone Bitters, no morphological changes in the colour of the organs however, the histological result revealed that at the dose of 500 mg/kg bwt, the drug may have affected the sperm production rate in the testis.[86] In addition, at 1 ml/kg, there was a significant increase in total bilirubin, conjugated bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and urea in the rats that received HB cleanser Bitters. A significant decrease was observed in the levels of total protein and albumin compared to negative control. Hence. HB cleanser Bitters may adversely affect hepatic and renal indices and therefore should be used with caution.[87]

CONCLUSION

The use of herbal medicine is gaining popularity due to the increasing prevalence of drug resistance in bacterial populations. While plant-derived medicine is believed to be safer than synthetic drugs and provides profound therapeutic benefits, polyherbal formulations should be seen as adjunctive therapies that can boost immunity against diseases, rather than as replacements for conventional antibiotic treatments. This comprehensive review has shed light on the various benefits of polyherbal formulations in terms of their antimicrobial, anti-inflammatory, antioxidant and toxicological properties. It is worth knowing that the formulations have been traditionally used in the treatment and management of various diseases. The reviewed studies have demonstrated the potential of polyherbal formulations as an alternative approach to modern medicine. They have shown great potential as sources of nutraceuticals with high therapeutic importance, and they could serve as a blueprint for future developments in the pharmaceutical sector. However, there is a need for further research to validate the efficacy and safety of these formulations, carry out more clinical studies, identify the active constituents responsible for their therapeutic properties, and standardize their preparation and dosage. With the increasing demand for natural remedies, this review provides useful insights into the potential use of polyherbal formulations in the development of new pharmaceuticals. The folklore system of medicine has led to a scientific revolution in nutraceuticals and phytopharmacotherapy, and the use of polyherbal formulations is likely to increase in the future. This review serves as a valuable resource for researchers, healthcare professionals, and the general public interested in the potential benefits of polyherbal formulations.

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