

Review Of Phytomedicine and Its Potential Contribution to Wound Healing

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Abstract: In the present scenario phytomedicines are in great demand in the developed world as they are able to cure many contagious diseases. These herbal drugs provide exceptional contribution to modern therapeutics. These herbal drugs are gaining importance from both practical and scientific view point. Their efficacy proved for primary health care because of their safety and lesser side effect. The new-found popularity is due to their almost miraculous success with the cases which were given up as hopeless by allopathy system of medicine. The amalgamation of phytomedicine into the health system needs to be developed in such a way to bring harmony between the traditional and modern system of health care. The present review deals with the impact of phytomedicines in wound healing in the present scenario.

Keywords: Phytomedicines, Wound healing, Primary health care system, Allopathy system, Aloe-vera

INTRODUCTION

About a quarter of all U.S. pharmaceutical prescriptions include at least one chemical originated from a plant at this time. There have been around 121 medicinal products based on traditional knowledge from diverse sources developed in the past century. In folklore and ancient systems of medicine, plant material was used as an indigenous remedy for a variety of ailments. Healing and strengthening of body systems (particularly the immune system which can then appropriately resist foreign invaders) and destroying infections without damaging side effects are currently the focus of herbal medicine or phytomedicines. Herbal medicines have been used in Chinese medicine from 2800 BC, according to historical records. Since many individuals prefer herbal treatment over synthetic medication, it has grown into a distinct sector today. About 5000 years ago, they were used by the Indians and Chinese, Egyptians and the Greeks, Romans and Syrians. Ancient scriptures describe over 500 therapeutic plants, while indigenous systems of medicine employ about 800. There is a wealth of traditional knowledge and medicinal plants in the Indian subcontinent, making it a great place to study medicine. Several plant species are used in indigenous systems including Siddha, Ayurveda, Unani, and Allopathy to cure various diseases (2). There are more than 80,000 plant species in use across the globe. More than 500 traditional groups in India employ roughly 800 plant species to treat various ailments, despite the fact that over 20,000 medicinal plant species have been documented (3)(4). First line primary health care for human relief relies on plant-derived medication, which has no side effects. Traditional remedies, over-the-counter pharmaceuticals, prescription drugs and dietary supplements are all examples of contemporary regulatory approaches for herbal medicines. Harmonization and improvement in the regulating process is required that incorporates scientific research and traditional wisdom. It will be feasible to get consistent and high-quality raw materials, which are crucial to the efficiency as well as the safety of herbal medicines because of the growing tendency toward domestication, producing biotechnological research as well as genetic development of medicinal plants.

S.no.	Drug	Basic investigation
1	Codeine, morphine	Ancient Sumerian utilize opium, a latex from the papaver somniferum plant. Greeks and Egyptians used it to cure arthritis, sleep disorders and headaches.
2	Atropine, hyoscyamine	In Babylonian legend, key medication, includes atropa belladonna, Hyoscyamus Niger etc.
3	Ephedrine	Ephedra sinica is a crude drug (Astringent yellow) that has been used by the Chinese for respiratory disorder since 2700 BC.
4	Quinine	The preuvian Indian plant cinchona spp. Is used to cure fevers.

5	Emetine	Native Americans from Brazil and other south American tribes utilised the rhizomes and roots of cephaels spp. to cause vomiting and treat dysentery.
6	Colchicine	Since 78 ADS, colchicum has been utilised in the treatment of gout through Europe.
7	Digoxin	During the 18 th century, Europe employed digitalis leaves in cardiac treatment.
8	Artemisinin	Chloroquine- resistant malaria has been treated with a drug discovered in China from Artemisia annua L and its derivatives.

PHYTOCHEMICALS:

BIOLOGICAL BACKGROUND

All plants generate chemical molecules as a natural part of their metabolite's carbohydrates and fats –which are present in all plants as well as the secondary metabolites sugars and sterols. Which are only found in a small number of plant species or genera. The secondary metabolites and pigments are those that can be processed into medications and have therapeutics effects in humans. These plant-based medicines or phytomedicine, are effective in the human's body plants responds to a local assemblage of herbivore, pollinator and microbial species by upregulating and downregulating certain biochemical pathway [4]. A single plant's chemical profile may change over time as it adapts to changing environmental conditions. In spite of the fact that plants produce an incredible number of phytochemicals, most are the result of a few basic biochemical principles. There is a discussion of some of the phytochemicals that could be useful in the development of plant-based medicines.

Alkaloids

The nitrogen ring is present in alkaloids. There are a large number of alkaloids that have significant effects on the nervous system. Caffeine is an alkaloid that gives you a slight boost, but the alkaloids in Datura can make you extremely drunk or even kill you if consumed in large quantities. A few of the alkaloids are hyoscyamine (Datura stramonium), atropine, cocaine, codeine and morphine.

Terpenoids

Terpenes are the building blocks from which terpenoids are constructed. Two isoprene pairs make up each terpene. Monoterpenes are responsible for the scent of roses and lavender. Pumpkin, corn, and tomatoes all have reds, yellows, and oranges because of carotenoids. Tetrahydrocannabinol (Cannabis sativa), Azadirachtin (Neem tree) and Artemisinin (Artemisia annua Chinese wormwood) are some of the other common terpenoid terpenoids.

S. No	Plant Name/Family	Drug
1	Catharanthus roseus L. (Apocynaceae)	Vinblastine & Vincristine
2	Podophyllum emodi wall (Berberidaceae)	Podophyotoxin
3	Taxus brevifolia (Toxaceae)	Paciltaxel, Taxotere
4	Mappia foetida miers	Comptohecin and Irenoteccan
5	Comptothea acuminata	Quinoline and Comptohecin alkaloids
6	Juniperus communis L. (Cupressaceae)	Teniposide and etoposie

The Healing Power of for Skin Wounds



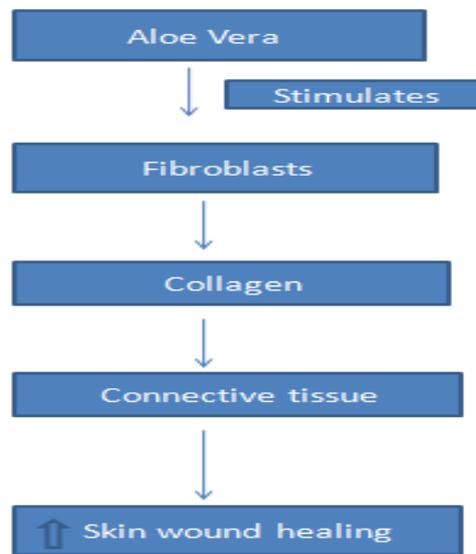
Aloe Vera

Aloe Vera is a tropical herb with a wide geographic distribution that grows well in hot, dry areas. The mucilaginous centre of an A. vera leaf can be used to extract gel. It has been used for millennia and is a main component in many commercial skins and burn

wound care treatment. A. Vera gel contains enzyme, polysaccharides, amino acids, carbohydrates, minerals, vitamin A, B, C, and E as well as. According to study, the glycoprotein fraction extracted from Avera promotes cell motility and proliferation [15] [16].



Mode of Action



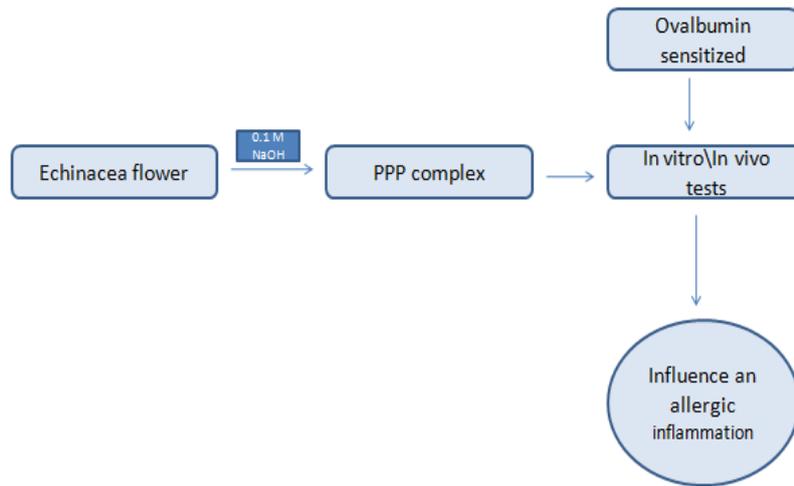
Echinacea

The herb Echinacea and the chemical echinacoside that makes up it appear to have good anti-inflammatory and tissue healing qualities. A coffee oil conjugate made from Echinacea called echinacoside has anti hyaluronidase properties that have been scientifically validated. Echinacea’s role in wound healing was investigated by Rousseau et al who also examined the herb’s ability to inhibit the enzyme hyaluronidase in pig’s vocal cords. 300, 600 and 1200 mg of standardized Echinacea were applied topically at random to the afflicted side

The results showed that anti hyaluronidase therapy was effective in hastening the recovery of vocal cords.



Mode of Action

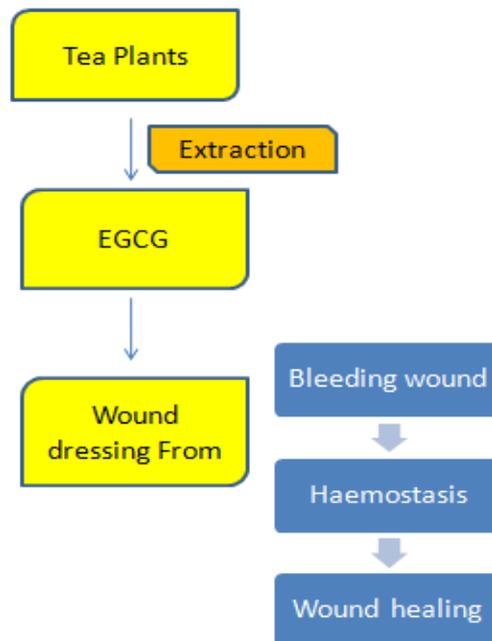


Green Tea

Green tea contains a high number of polyphenols, the most important of which being catechin gallate [10]. When the collagen gel that fibroblasts have colonized contracts, they alter the properties of TGF β 1. This is thought to be connected to the epigenetic of vascular endothelial growth factors and the development of myofibroblasts. Tea may therefore facilitate faster wound healing [11].



Mode of Action

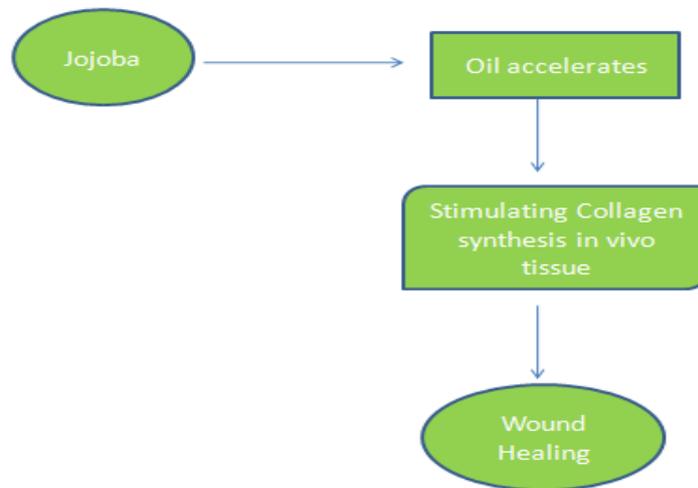


Jojoba

Simmondsia chinensis, also known as jojoba, is a dry, perennial plant that is cultivated in some regions of the United States and Africa [12]. Liquid jojoba waxes increased fibroblasts production of collagen I in In vitro tests on human keratinocytes; it had no effect on the release of matrix metalloproteinase 2 and metalloproteinase. As a result, jojoba might promote quicker wound healing [13].



Mode of Action

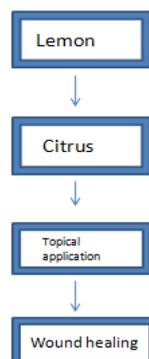


Lemon

As a result, wounds may be treated in the therapeutic context using it [14]. A great source of vitamin C (ascorbic acid); lemons are a delicious way to get your daily dose. In diabetic Wistar rats, we looked at the role vitamin C played in wound healing. As an antioxidant and anti-apoptotic agent, vitamin C aids in the healing of skin wounds [15].



Mode of Action



Soyabean

The immune system of burn victims treated with soybean suspensions was studied by researchers. All populations of immune-competent cells, including T helper lymphocytes, were shown to be stimulated by soy including those responsible for repair functions, antibodies, and anti-inflammatory cytokines. Black soybean seed coat anthocyanins have anti-inflammatory and antioxidant effects. Anthocyanins have been shown to improve Sprague Dawley rat wound healing. The cytoprotective, angiogenesis-enhancing, and anti-inflammatory characteristics of anthocyanins can promote wound healing. Herbal remedy for treating contusions using the root of comfrey (*Symphytum officinale* L.) This herbal supplement is thought to include allantoin, a pharmacologically active component. The pharmacological action of allantoin 5 ureide hydration include the removal of necrotic tissue, induction of cell mitosis and promotion of epithelial stimulation. According to Araujo et al., allantoin in an oil/water(O/W) emulsion soft lotion promotes wound healing in comparison to the control group. [16]. However, it isn't as potent as the literature portrays it to be. It is via the management of inflammatory responses and the encouragement of both fibroblast proliferation and extracellular matrix synthesis that allantoin stimulates the healing process.



Mode of Action

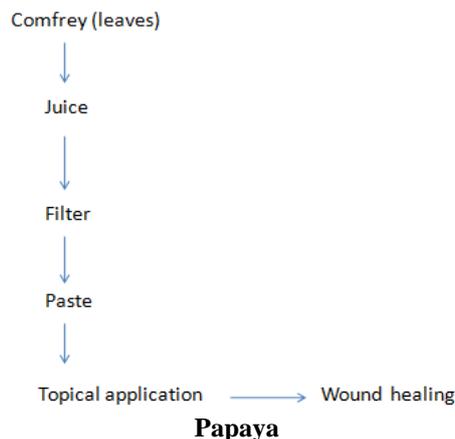


Comfrey

Comfrey leaf extract was used in an experiment to see whether it may help heal wounds. Carbomer gel, glycerol alcohol solution, and O / W emulsion (soft lotion) were examined in terms of their topical compositions. It has been shown that O/W emulsions are best for promoting healing activity. Collagen deposition increased from 40% to 240 percent and inflammatory cell infiltration decreased from 3% to 46% from day 3 to day 28. However, the greatest results were obtained using an emulsion-prepared 8 percent extract [17].



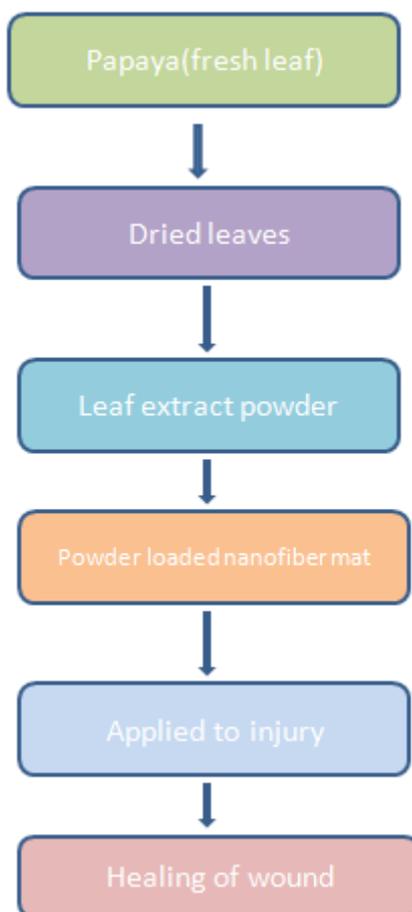
Mode of Action



Papaya supplements have been shown in studies to improve wound healing and lessen the severity of local inflammation in rats with burns. This plant inhibits the bacterial enzyme catalase, which improves the capacity to eliminate intracellular microorganism. Papaya's antioxidant qualities also aid in preventing oxidative damage tissues. Sprague Dawley rats were injected with an ethanol extract of carica papaya seeds (50 mg/kg/day) to test for wound healing qualities in animal studies. Granulation tissue had a greater concentration of hydroxyproline. The collagen deposition in granulation tissue was well-organized, according to histological examination. Salmonella choleraesuis and Staphylococcus aureus were shown to be resistant to the extract's antibacterial properties [18].



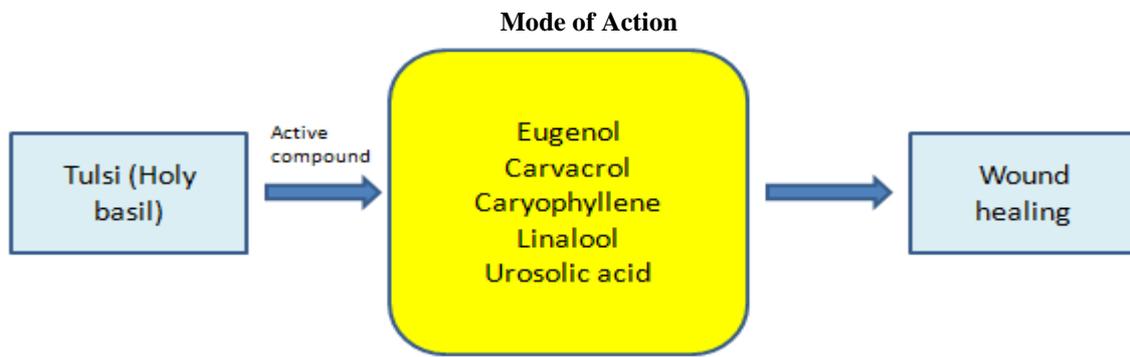
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Ocimum

Ocimum (Holy Basil) is an herb used in Indian medicine that has a number of medicinal qualities, including the ability to heal tissue and the activation of cytokines. The administration of 10% Ocimum sanctum extract to petrolatum increased the rate of epithelialization and wound constriction in Wistar albino rats in vivo. O. Sanctum may assist both keloid scars and hypertrophic scars. A study by the researchers of Udupa et al found that dexamethasone-suppressing healing in albino rats was inhibited by an ethanol extract of O. Sanctum. Even more surprisingly, they discovered that compared to control groups, the wounds healed faster swiftly and closed more quickly. The amounts of hydroxyproline and granulation tissue also increased [19].





Rosemary

When it comes to aromatherapy, rosemary (*Rosmarinus officinalis*) oil is one of the most popular. In an in vivo investigation, diabetic BALB/c mice had two full-thickness circular wounds made in the dorsal region. The wounds of diabetic mice were treated with *R. officinalis* essential oil for three days. Angiogenesis and regeneration of granulation tissue were also seen in the treated wounds [20], as was collagen deposition and a reduction in inflammation [20].



Mode of Action



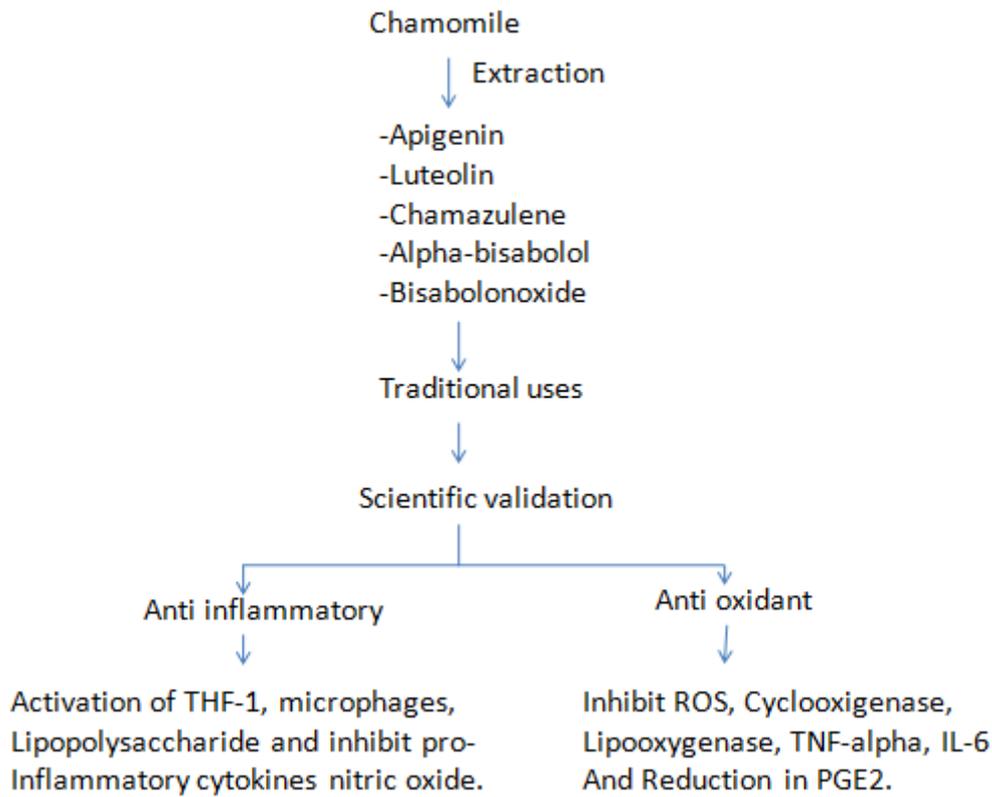
Chamomile

Chaste tree flower (*Matricaria*) is rich in essential oils and flavonoids that contribute to the plant's medicinal properties. Wounds may be treated with chamomile extract and decoction.



Recent research suggests that chamomile heals wounds more quickly than corticosteroids, an interesting finding. Additionally, chamomile has an antiulcerogenic effect as a result of its ability to block H₂ receptors. Antagonists of the 5-hydroxytryptamine-2 (5-HT₂) receptor help to restore the epidermal barrier and enhance wound healing. Chamomile has been shown to have opioid-like effects. Wound healing is accelerated and platelet aggregation is boosted by topical opioids. Topical chamomile has been shown to improve wound healing in individuals who have had dermabrasion for tattoo removal [21]. They found chamomile to be statistically effective in drying wounds and speeding up re-epithelialization.

Mode of Action

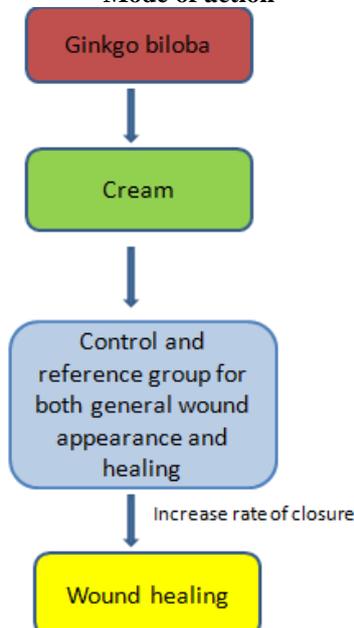


Ginkgo

The Ginkgo biloba tree is said to be the world's oldest surviving species. The healing suppressive activity of cyclophosphamide was in G. biloba extract. They were able to demonstrate that G. biloba improved granulation breaking strength and hydroxyproline amino acid.



Mode of action



Higher-Plant Botanical Medicine

Modern medicine has been significantly influenced by herbal treatments. For instance, the treatment of hypertension was revolutionized when rauwolfia serpentine's serpentine root was discovered in 1953. Approximately 100 new herbs, mostly derived from higher plants like deserpidin, reseinnamin and reserpine were released to the US pharmaceutical market between 1950 and 1970. In the years between 1971 and 1990, medicine like ectoposides, guggulsterone, teniposides and nabilones were made available all over the world. Also, around this time, ginkolides were first introduced. Only 2% of new medication were introduced between 1991 and 1995, and they included paclitaxel, topicon, hominin and irinotecan. Chorionic lymphoma, Hodgkin's lymphoma, non-lymphoma, Hodgkin's and testicular and neck cancer are all treated with vinblastine isolated from *Catharanthus roseus*. Among the many conditions for which vincristine is prescribed are acute lymphocytic leukaemia in children, Hodgkin's disease in its advanced stages, lymphosarcoma, small cell lung cancer, and cancers of the cervix and breast. Podophyllum emody, which includes podophyllotoxin, is being used to treat lymphoma, small cell lung cancer and testicular cancer. *Nothapodytes nimmoniana* (*Mappia foetida*) is the main cause of cervical cancer in Japan. Since ancient times, herbalists have utilized this plant to cure a wide range of illness, including hepatitis, cancer, rheumatoid arthritis, depression and anxiety. More than 64 plants were identified to have antibacterial capabilities were discovered in antidiabetic herb, plants studies and the ability to use an Indian root extract to neutralize the toxin of *Naja kaouthia*. It successfully neutralized the pathophysiological alterations brought on by the toxins of *hemidesmus indicus* R. Br and *Daboia russellii* [22]. The disease is currently treated with a wide variety of medications.

PHYTOMEDICAL RESEARCH AND METABOLOMICS Objective and reliable methods must be used to ensure that the chemical profile's content is reproducible. For this purpose, an innovative method called metabolomics has been implemented. It is expected that plant metabolites will be more complex than those of mammal medicinal plant compounds.

METABOLOMICS IN PHYTOMEDICAL RESEARCH

Regulatory agencies are requesting research into new analytical methods to more rigorously standardize botanical medicines to improve the accuracy and consistency of globally controlled botanical medicines. These methods must be objective and reliable and must also ensure the reproducibility of the content of the chemical profile. In comparison to human metabolites, plant metabolites are anticipated to be considerably more complicated.

ROLE OF WORLD HEALTH ORGANIZATION

According to the world health organization (WHO) natural medicine is presently used for certain aspects of primary fitness care by seven billion people, or 80% of the world's population. Along with the growing trends of using natural remedies as treatment for common ailments, there may also be a growing worry regarding their efficacy, safety and management [23]. As a result, the WHO was compelled to provide recommendation for manipulating in the 1993 Publication'' research guideline for evaluating the safety and efficacy of herbal medicines''. The guidelines are equally serves as those that apply to tablets in general. Traditional, complementary and alternative medicine (TCAM) has been recognised by the WHO for the past 30 the most effective culturally acceptable affordable and sustainable form of health care. In order to discuss method for the selection and application of conventional medicines in national primary health care (PHC) programmes, WHO has organised interregional seminars, the world-wide fund for nature the international union for the protection of nature and natural resource, and who advocated ideas for protecting medicinal plants. There in large plan include maintaining the exiting order botanical gardens as well as preventing the loss of forests and related species [24]. WHO's traditional medicine programme aspires for people to use reliable and potent agrocommercial technology in the production of natural medicine and the cultivation and processing of medicinal plants in order to establish vast distribution networks for seeds and plants. According to the WHO, out of 119 medicines generated from plant, around 74% are used in modern medicine in ways that immediately match with their traditional uses as pharmaceuticals developed from plants with the aid of local culture. For their potentials medicine effects, major pharmaceutical firms are now doing extensive research on plant compounds sourced from the rain forest and other places. The 6th international conference of drug regulatory authorities, which held in Ottawa in the same year and advanced similar rules reaffirmed then. In 1991, WHO advanced criteria for the evaluation of natural medicines.

METABOLOMICS IN PHYTOMEDICINE RESEARCH

The regulatory authorities throughout the globe are asking for investigations into novel analytical methods to tighten the standardisation of phytomedicines in order to improve their accuracy and consistency. Such methods must be both objective and robust, and they must be concerned with the repeatability of the chemical profiles' content. As a new and cutting-edge approach to meeting these needs, metabolomics has been used. Metabolomes of plants are expected to be even more complex than those of mammals. The metabolomes of medicinal plants are particularly helpful in the development of new phototherapeutics and nutraceuticals based on evidence. Drug metabolism, toxicity, and disease progression may all be tracked using comparative metabolomics structures. Paclitaxel (taxol), camptothecin (irinotecan, topotecan), and podophyllotoxins are all well-known secondary metabolites of the plant that are used in cancer chemotherapy tablets (etoposide, teniposide). The remarkable potential of plant secondary metabolites or herbal products to function as health care items or as lead molecules for the creation of novel medication has renewed interest in pharmaceutical and nutraceutical research. By enabling researchers to separate out certain active Phyto compounds, the early 19th century discovery of morphine from opium ushered in a new age of drug development. Due to their low abundance in vegetation, single active Phyto compounds are occasionally only weakly detectable in this reductionist approach, or a spectrum of therapeutics efficacy previously discovered arises most effectively as a synergistic fueloline chromatography, high overall performance liquid chromatography, and nuclear magnetic resonance are the primary methodologies for evaluating target compounds and metabolic profile, and they are utilising (NMR). Furthermore, metabolomics employs a wide range of complementary analytic methods, including LC/MS, LC/MS, and LC/NMR "hyphenated" methodologies. These procedures rely on chromatographic separations and frequent calibrations for specific analytes, both of which require a high level of sophistication. NMR, direct injection mass spectrometry (MS), or Fourier transform infrared spectroscopy may be used to analyse crude extracts without the need for separations.

EXPERIMENTAL EVIDENCE

As a purgative, *Curculigo Pilosa* is often used in South-western Nigeria for hernia, infertility, and gonorrhoea treatment. It is also used to prevent and treat these conditions. Alkaloids, saponins, tannins, cardenolides, and anthraquinones are among the phytochemicals found in *C. pilosa*. An anticandidal effect was seen with the ethanol extracts (500 mg/ml) and undiluted crucial oil, however the water extract (a thousand mg/ml) became ineffective against isolates. The ethanol extract's MIC ranges from 0.020 to 1.500 mg/ml when used against the tested isolates. As a consequence, *C. pilosa*'s active components might lead to the development of anticandidal phytomedicine. Ethanolic extracts of *Alchornea cordifolia* leaves were isolated and analysed to determine the plant's form [26]. Use of NMR spectroscopy in combination with infrared and mass spectrometry data for Mull. Arg, 5-methyl four'-propenoxy anthocyanidines, 7-O-D - diglucopyranoside. *Pseudomonas aeruginosa*, *E. coli*, *P. mirabilis*, *K. Pneumonia* and *S. aureus* were all successfully suppressed by the remoted compound in antibacterial studies. Use in phytomedicine to prevent and treat infections is supported by this study [27].

RESEARCH HURDLES IN PHYTOMEDICINE

Though the efficacy of natural medicines has been well-documented over many decades, the mechanism by which they move through the human body, as well as the associated products derived from nature, is far more difficult to understand than the mechanistic rationalisation of a single bioactive factor. This is due to the fact that the extracts used are either unfractionated or partially fractionated. Components are frequently used in conjunction with one another. Regardless of the situation, synergism is almost always playing a critical role. It may be difficult to evaluate and isolate those mixtures of the active constituent and their mode of movement. Besides that, a possible far-reaching remark has been made in regards to the safety of ingesting positive herbs. For the first time in history, researchers of herbal products may have to be more flexible than ever [28].

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