



NEW TRENDS IN HERBAL FORMULATIONS AND DRUG DELIVERY SYSTEMS: A REVIEW

Sherry Sebastian ¹, Rosna Babu ², Vidya Peter³

B Pharm Scholar ¹, B Pharm Scholar ², Assistant Professor ³

Department of Pharmaceutics,

Nirmala College of Pharmacy, Muvattupuzha, Ernakulam, Kerala, India.

Abstract: Herbs are a widely distributed and widespread group of plants, with leaves, seeds, or flowers used for flavoring, food, medicine, and perfume. One sort of dietary supplement is herbal medicine. They are sold as tablets, capsules, powders, extracts, and in novel dosage forms. Herbal remedies are used by people to maintain or improve their health. Many people believe that products labeled “natural” are always safe and good for them. Herbal medicines are of great demand in this developed world because of their cultural acceptability, better compatibility, efficacy, safety, and less side effects. Herbal preparations contain only purified ingredients and are regulated by the FDA. Herbal supplements can include whole plants or portions of plants. Herbs which are in dried or in fresh form are extracted and further processed for preparations such as infusion, decoction, maceration and distillation. In this article we attempt to discuss various conventional and novel herbal preparations which are the basis for new herbal products.

Index Terms: Herbal medicine, Herbal Dosage Forms, Scope, Herbal Extracts, Novel Formulations, Limitations, Advantages.

Introduction:

Herbal formulations or medicines are now widely used, even though some conflicts exist between herbal medicines and customary pharmacological medicines. These formulations have got good acceptability as they contain therapeutically active agents like nootropics, anti-diabetics, hepatoprotective agents and lipid-lowering agents. These formulations consist of one or more herbs or processed herbs in specified quantities to provide specific nutritional or cosmetic benefits. They are meant for use to diagnose, treat or mitigate diseases of both human beings and animals. They usually contain active substance such as, herbal substances, herbal preparations, combination of herbal substance with herbal preparations. ^[1]

Scope of Herbal Formulations:

The use of herbal formulations to treat a variety of disorders has found widespread use in the pharmaceutical health care system. Phytotherapy has been used for a long time over thousands of years. [2] Another factor for the increase in market share and popularity is the introduction of herbals in the form of dietary supplements and nutraceuticals. As evidenced by an expanded market for herbal medications, the usage of phytotherapeutics has increased dramatically among patients and clinicians. [3] Herbal medications are in significant demand for primary health care in both developed and developing countries because of their broad biological activities, higher safety margins, and lower costs. The therapeutic effect of herbal medications is based on the overall function of a range of active components, since all ingredients work together to generate synergistic action. [2]

The majority of herbal formulations in the market are polyherbal, meaning they contain a range of active ingredients, all of which work together to enhance the therapeutic effectiveness. Each active ingredient in the polyherbal formulation has a distinct role to play, and they are all interconnected. [4] After the active component has been isolated, the chemical synthesis and large-scale manufacture take several years. Herbs are manufactured in a variety of modern dosage forms, including tablets, capsules, topical creams, gels, and ointments, as well as some unique drug delivery forms, such as prolonged release and microencapsulated dosage forms. [5]

The various herbal formulations consist of:

1) Conventional Formulations

1.1. Infusions

Infusion is the process of extracting chemical compounds from a material in a highly soluble solvent such as water, oil, or alcohol by allowing the cloth to remain suspended in the solvent for an extended period of time. They are typically used with delicate herbs, leaves, and young sensitive plants. The *in vitro* anti-proliferative activities of tea and flavourer infusions showed that some infusions powerfully smothered the proliferation of human carcinoma cells and attenuated the viability of those neoplastic cell lines in an exceedingly dose-dependent manner. [6]

1.2. Decoctions

Decoctions are usually the method preferred when working with tougher and more fibrous plants, barks and roots etc. (and which contain water soluble chemicals). Instead of just steeping the plant material in hot water, it is cooked for a longer amount of time. The water decoction of a mixture of two to twelve herbal materials is one of the most common traditional herbal dosage forms. [7] The studies have shown that decoction of dingjifumai useful to treat ventricular arrhythmia, and it has provided a very good curative effect. However, the anti dermatophyte activity of the decoction, extract was very low compared with the hydrolysed mixture of the same. [8]

1.3. Tinctures

Tincture is an alcohol and water extract which is used when plants contain active chemicals that are not much soluble in water, or when a large quantity is to be prepared for convenience and long term storage is required. [9] Most of the plant constituents dissolve easily in a mixture of alcohol and water rather than in pure water. The finished extract needs an alcohol content of at least 20 % v/v to adequately preserve it. [10] The right concentration of ethanol is required for maximizing the quality of the herbal preparations. [11]

1.4. Poultices and Compresses

A poultice, is a soft, moist mass, often heated and medicated, that is spread on a cloth and placed over the skin to treat an aching, inflamed or painful part of the body. There were various methods for the preparation of poultices. It can be made by mashing fresh herbs.^[12] A light cotton bandage is used to bind the poultice to the affected area. Poultices may be used externally to relax muscles or to ease minor skin eruptions, poison ivy, insect bites, superficial wounds, and inflammation.^[13] Compresses are prepared by simply soaking a cloth in a prepared infusion, tincture or decoction and laying the same onto the affected part of the body.^[7]

1.5. Herbal glycerites

Glycerite is a fluid extract of an herb or different medicinal substance that could made use of glycerin as the bulk of the fluid extraction medium. Their preparation is similar to that of tinctures but in this case, glycerine is used in the extraction process instead of a mixture of alcohol and water.^[12] Glycerine is considered as a good preservative for fresh plant juices, wherein half of plant juice and half of glycerine are mixed, as it keeps the juice green and in suspension better than alcohol. This sort of preparation is known as succus and for soothing preparations intended for the throat and digestive tract, or coughs.^[11]

1.6. Herbal capsules

Capsules are solid dosage forms containing drugs and fillers enclosed in a gelatin container.^[14] They are available in hard gelatin for dry powdered herbal ingredients or granules and soft gelatin shells for herbal ingredients that are dissolved or suspended in oil. Drugs are usually more readily released from capsules compared to tablets.^[13] The herbal capsule preparations have relatively better stability compared to aqueous preparations such as decoctions and infusions.^[15] The preparations can be used for treatment of various ailments, including *Barosma betulina* for cystitis, *Allium sativum* for hypertension, *Zingiber officinale* for hyperacidity etc.^[16]

1.7. Herbal ointments

An ointment is a homogeneous, viscous, semi-solid preparation, usually greasy, thick oil (oil 80% and water 20%) with a high viscosity that is intended for external application to the skin or mucous membranes. Ointments have a water number that defines the maximum amount of water that they can contain. The base is usually selected should be anhydrous (hydrophobic) and immiscible with skin secretions.^[14] Ointments are usually used as emollients or to apply suspended or dissolved medicaments to the skin.^[15] Herbal ointments normally have the plant material(s) either in finely sifted or extracted form which are incorporated into the base.^[17] These ointments should not be used for deep wounds.^[18] Ointment formulations can be used for sore legs, burns and scalds and for scabies.^[19]

1.8. Herbal creams

Creams are semi-solid emulsions that are oil-water mixtures. They are viscous semi-solid preparations which may be either oil in water type (aqueous cream) or water in oil type (oily cream). They have antimicrobial preservatives due to the presence of water in the base, but have comparatively shorter shelf life than ointments.^[17] Many people tend to confuse creams and ointments as the difference arises only in the nature of base. Herbal creams are those which have a hydrophilic base on the other hand, if the base is purely hydrophobic, then the preparation must be qualified as an ointment.^[15]

1.9. Herbal soaps

Soap is a salt of a fatty acid prepared by saponification of a fatty acid with a suitable base (such as caustic soda).^[20] It is generally prepared by mixing fats and oils with a base. Herbal soaps have the herbal materials incorporated in the detergent base. These herbal materials usually have an antifungal and antibacterial effect on the skin and can also help in cleansing of the skin. They are normally used for microbial skin conditions such as dandruff, eczema, ringworm and boils. The shelf-life of soaps can be increased by adding preservatives or antioxidants.^[21]

1.10. Herbal Pastes

Pharmaceutically, topical pastes are ointments which may contain about 50 % powder dispersed in a fatty base.^[14] They usually localize the action of irritant or staining materials and are less greasy compared to ointments.^[15] Herbal pastes may contain the herbal ingredient dissolved or dispersed in a base (fatty base if it is meant for topical use or a more aqueous stiff base if it is meant for oral use as is done in herbal toothpaste). Special care should be taken to ensure that herbal oral pastes contain only herbal materials that are safe for oral use.^[22]

TABLE 1: Some examples for conventional herbal formulations

| Formulations | Category | Constituents | Uses |
|---------------------------------------------------------------|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| Priyasan-jeevini adivasi Herbal Hair Oil | Hair oil | Coconut milk, Bringraj leaves, Aloe vera gel, Neem leaves, Brahmi leaves, Hibiscus leaves, Tulsi leaves, Henna leaves | Used for Dandruff, prevent hair fall and split ends |
| Sleep support | Herbal capsules | Tagara, Valerian root, Chamomile, L-Theanine, Tryptophan, L-Threonine | Calm nerves, reduce anxiety, and promote quality sleep. |
| Tejasvi brightening emulsion | Herbal cream | Saffron, Kasturimanjal, Desighee, Sweet almond oil | For rejuvenated, plump and radiant skin conditions. |
| Medimix Clear Glycerine Soap | Herbal soap | Sodium Lauryl Ether Sulphate, Stearic Acid, Glycerine, Sodium Hydroxide, Lauric Acid, PEG 400, Perfume, Light Liquid Paraffin, Edta Di Sodium Salt, Herbal Extracts, Aloe Vera | Energize skin and keeps skin moisturized. |
| Lever ayushanti-Cavity Natural Ayurvedic Clove Oil Toothpaste | Herbal paste | Clove Oil, dasanakanthichoornam, Turmeric (Haldi), Saffron (Kesar), Cows ghee, Cardamom and Rock Salt | Powerful antibacterial quality relieves toothache, bleeding gums |
| Himalaya active fresh gel toothpaste | Herbal paste | Indian Dil, Fennel, Miswak Clove, Cardamom, Menthol | Effective against dental caries, provide fresh breath |
| Herbal Balm, Ayubal Wellness, Non prescription | Herbal balms | Aloe veraraspudina sat kapoornilgiri oil | Relieves tension headaches, removes back pain, neck and shoulder tension, removes joint pain. |

2) Novel Formulations

Most of the herbal formulations have low bioavailability. The limitation can be overcome with the use of novel delivery systems like phytosomes, liposomes, marinosomes, niosomes and photosomes etc. These systems can enhance the rate of release as well as the capacity to cross the lipid rich bio membranes and thereby effectively addresses the limitations of a traditional drug delivery system. [16]

2.1. Phytosome

Phytosomes are advanced forms of herbal products that are better absorbed, utilized, and can produce better results compared to conventional herbal extracts. The recent technology of drug delivery when applied to herbal drugs and phytoconstituents will open new avenues to explore the maximum therapeutic potential of plant substances of polar nature. [23]

2.2. Niosome

These are microscopic, the lamellar structure of the novel drug delivery system in which the herbal drug is encapsulated in a vesicle. Niosome surfactants are biodegradable, biocompatible and non-immunogenic. The drug delivery by transdermal route, however, appears to show that the more fluid membranes appear to be more efficient. Vesicle size has not been fully characterized and studies designed to systematically define the size requirement for certain pharmacodynamic objectives which are desired for the research purpose. [24]

2.3. Liposomes

Liposomes are spherical shaped, self closed vesicles of colloidal dimensions. They contain phospholipids bilayer which sequesters part of the solvent, in which they freely float, into their interior. [25] In the case of one bilayer encapsulating the aqueous core may be either of small or large unilamellar vesicles while in the case of many concentric bilayers one defines only large multilamellar vesicles. [26]

2.4. Marinosome

These are liposomes made from a natural marine lipid extract was used for the prevention and treatment of skin diseases. At low pH or in the presence of high calcium concentrations, complex structural rearrangements can occur, such as aggregation and size reduction, which were kinetically dependent on conditions. [27]

2.5. Photosome

Photosomes consist of photolyases (a bacterial enzyme that can repair ultraviolet B (UVB)- induced cyclobutane pyrimidine dimers (CPD) in eukaryotic cells) which are included in liposomes. Photolyases are specific enzymes that can bind to the lesion and reverse the damage with the energy of light by photo reactivation. Photolyases are monomeric flavoproteins of 50–60 kda and contain two chromophores as cofactors. These photo reactivating enzymes uses the energy of near UV/visible light (300–500 nm) to repair directly and effectively CPD or 6-4 photoproducts. [28]

2.6. Transferosomes

Transferosomes are a form of elastic or deformable vesicle which is made up of soya phosphatidyl choline incorporating sodium cholate and a small concentration of ethanol. They are applied in a non-occluded method to the skin and have been shown to permeate through the stratum corneum lipid lamellar regions as a result of the hydration or osmotic force in the skin. [29] It has been used successfully as carriers for a range of drugs, including steroids, NSAIDs and local anaesthetics. [30] Higher membrane hydrophilicity and flexibility both help transferosomes to avoid aggregation and fusion, which are observed with liposomes exposed to an osmotic stress. [32]

2.7. Nano emulsions

Nanoemulsions are isotropic dispersed systems of two immiscible liquids. They consist of an oily system dispersed in an aqueous system, or an aqueous system dispersed in an oily system. Esters derived from Palm kernel oil to prepare nanoemulsions that were loaded with *Phyllanthus urinaria* extract. These were investigated for their antiaging effect and demonstrated DPPH radical scavenging activity, neutralizing reactive oxygen species and oxidative injury induced by ultraviolet radiation. ^[32]

2.8. Ethosomes

Ethosomes are flexible liposome, with alcohol incorporated into the lipid bilayer to give the structure their flexibility. Hydrophilic, lipophilic or amphiphilic drugs can be incorporated in ethosomes and these are able to reach the deeper skin layers and the systemic circulation formulated ethosomes using a combination of Vitamin A, Vitamin E and Vitamin C. ^[33]

2.9. Microspheres

Microspheres are spherical particles of 1-1000 μm size, in which the drug is uniformly dispersed in polymer matrix and gets released following first order kinetics. ^[34] A prolonged release of the drug for a period of 12 h was achieved, which resulted in increased bioavailability of the drug. ^[35]

2.10. Transdermal patches

The drug diclofenac diethylamine also possesses the ideal characteristics such as poor bioavailability (40–60%), short biological half-life (2–3 h), smaller dose (25–50 mg), etc., to be formulated into a transdermal patch. Transdermal patches offer added advantages such as maintenance of constant and prolonged drug level, reduced frequency of dosing, minimization of inter- and inpatient variability, self administration, and easy termination of medication, leading to patient compliance. ^[36]

TABLE 2: Examples for novel herbal formulations

| Formulations | Category | Constituents | Uses |
|-------------------------------------|---------------------|-------------------------------------------------|-------------------------------------------------|
| Forest sap detox foot patch | Transdermal patches | Tourmaline, Chitosan, Pearl Stone, Wood vinegar | Detoxification, Increase oxygen intake |
| Glycyrrhiza glabra-Nanoparticles | Saponin glycosides | Glycyrrhizic acid | Anti viral, anti-inflammatory, Anti-Hepatotoxic |
| Ginkgo biloba-nanoparticles | Flavonoids | Extracts of ginkgo Biloba | Brain function activation |
| Silibummarianum-nanoemulsions | Flavonolignans | Silymarin | Hepato-protective |
| Curcuma zedoaria-nanoemulsions | Resins | B-elemene | Hepato-protection Anticancer and antibacterial |
| Taxus brevifolia-microemulsions | Diterpene | Docetaxol | Anticancer |
| Pilocarpus Jaborandi-microemulsions | Amino alkaloid | Pilocarpine | Treatment of glaucoma |

Advantages of novel formulations of herbal extracts

Herbal medications offer a lot of therapeutic potential, and various value-added drug delivery strategies should be investigated. The solubility of lipids and the size of their molecules are the two most important factors for poor performance, low bioavailability and absorption. Standardized plant extracts or polar phytoconstituents such as flavonoids, terpenoids, tannins, and xanthenes have a considerably superior absorption profile when supplied using a new drug delivery vehicle, allowing them to permeate the biological barrier, resulting in increased bioavailability. Also, by novel formulations site specific controlled release can be made possible.^[37]

CONCLUSION

Medicinal plants are a great place to look for new pharmacological lead compounds. Phytogeographical differences, such as changes in ambient conditions, improper cultivation, and collection methods, interfere with medicinal plants' biological functions. Herbal medicines have contributed many of the most effective pharmaceuticals to modern medicine's large arsenal of drugs, both in crude form and as a pure chemical upon which contemporary drugs are based. The search for scientific data to back up tribal healers' claims about Indian plants has escalated.

People will be better informed about the effective pharmacological therapy and improved health status once these new ethno medicinal products have been professionally tested and communicated effectively. Although herbal medicines have many benefits, but they can have drawbacks. As a result, new disease-curing therapies must have low side effects and high effectiveness. Combining herbal treatments with allopathic pharmaceuticals has given the medical world a new lease on life.

REFERENCES

- 1) Adeyi AO, Nneji L. Ameliorative potentials of medicinal plants on the pathophysiological complications of diabetes mellitus: A review. *Journal of Medicinal Plants Research*. 2015 Feb 25;9(8):262-88.
- 2) Ekor M. The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Frontiers in pharmacology*. 2014 Jan 10;4:177.
- 3) Nasri H, Baradaran A, Shirzad H, Rafieian-Kopaei M. New concepts in nutraceuticals as alternative for pharmaceuticals. *International journal of preventive medicine*. 2014 Dec;5(12):1487.
- 4) Parasuraman S, Thing GS, Dhanaraj SA. Polyherbal formulation: Concept of ayurveda. *Pharmacognosy reviews*. 2014 Jul;8(16):73.
- 5) Katiyar C, Gupta A, Kanjilal S, Katiyar S. Drug discovery from plant sources: An integrated approach. *Ayu*. 2012 Jan;33(1):10.
- 6) Okore VC, Asogwa CI and Nnamani PO. Evaluation of antidiarrhoeal action of a hot-water infusion of *Ocimum gratissimum*, Linn. *Bio-research*. 7(1):2009; 422-425.
- 7) Leslie Taylor. *The healing power of rainforest herbs* (Square One Publishers, Inc.) 2004.
- 8) Chewchinda S, Wuthi-udomlert M, Gritsanapan W. HPLC quantitative analysis of rhein and anti dermatophytid activity of cassia fistula pod pulp extracts of various storage conditions. *BioMed Res Int* 2013.
- 9) Mazza G (ed.). *Functional Foods*. Technomic Publishing, Lancaster, PA, 1998.

- 10) Bone K. Dosage considerations in herbal medicine Part 3. *Mediherb Professional Review*; 1993.
- 11) Bruton-Seal J, Seal M. *Backyard medicine-harvest and make your own herbal remedies*. New York: Skyhouse Publishing; 2009
- 12) Bascom A. *Incorporating Herbal Medicine into Clinical Practice*. Philadelphia: F. A. Davis Company; 2002.
- 13) Hoffman D. *Medical Herbalism: The Science and Practice of Herbal Medicine*. Vermont: Healing Arts Press; 2003.
- 14) Winfield AJ, Rees AJ, Smith I. *Pharmaceutical practice*. London: Churchill Livingstone; 2009.
- 15) Aulton ME. *Aulton's pharmaceutics-the design and manufacture of medicines*. 3rd ed. London: Churchill Livingstone; 2007.
- 16) Ogbonna J, Kenekukwu F, Attama A, Chime S. Different approaches to formulation of herbal extracts/phytopharmaceuticals/bioactive phytoconstituents-a review. *Int. J. Pharm. Sci. Rev. Res.* 2012;16(1):1-8
- 17) Al-Achi A. *An introduction to botanical medicines: History, Science, Uses and Dangers*. Connecticut: Praeger Publishers; 2008.
- 18) Zdoryk OA, Khokhlova KO, Georgiyants VA, Vyshnevskaya LI. Investigation of physical and chemical stability of ointment with herbals. *Int J Pharm Compd* 2014;18:248-52.
- 19) Carson CF, Hammer KA, Riley TV. "Melaleuca alternifolia (Tea Tree) Oil: a Review of Antimicrobial and Other Medicinal Properties". *Clinical Microbiology Reviews*. 19(1): Jan. 2006; 50-62.
- 20) Jones M. *The Complete Guide to Creating Oils, Soaps, Creams, and Herbal Gels for your Mind and Body*. Atlantic Publishing Company; 2011.
- 21) Grosso A. *The Everything Soapmaking Book: Learn How to Make Soap at Home with Recipes*. Massachusetts: Adams Media; 2013.
- 22) Van Loveren C. *Toothpastes*. Amsterdam: Karger Medical and Scientific Publishers; 2013.
- 23) NS Acharya, GV Parihar, SR Acharya. Phytosomes: novel approach for delivering herbal extract with improved bioavailability. *Pharma science monitor An Int. J. of Pharm. Scs* 2(1):2011; 144-160.
- 24) John G, Sinha P, Rathnam G, Ubaidulla U, Aravind R. A Review on Future Prospects of Niosomes towards Drug Delivery Applications.
- 25) Noothi S, Maheswari K. LIPOSOMES: AS TARGETED DRUG DELIVERY SYSTEM.
- 26) Brandl M. Liposomes as drug carriers: a technological approach.
- 27) Moussaoui N, Cansell M, Denizot A. Marinosomes®, marine lipid-based liposomes: physical characterization and potential application in cosmetics. *International journal of pharmaceutics*. 2002 Aug 21;242(1-2):361-5.
- 28) Ramírez N, Serey M, Illanes A, Piumetti M, Ottone C. Immobilization strategies of photolyases:

- Challenges and perspectives for DNA repairing application. *Journal of Photochemistry and Photobiology B: Biology*. 2021 Feb 1;215:112113.
- 29) Bhardwaj V, Shukla V, Singh A, Malviya R, Sharma PK. Transfersomes ultra flexible vesicles for transdermal delivery. *International journal of pharmaceutical sciences and research*. 2010;1(3):12-20.
- 30) Biju SS, Talegaonkar S, Mishra PR, Khar RK. Vesicular systems: an overview. *Indian journal of pharmaceutical sciences*. 2006;68(2).
- 31) Cevc G, Gebauer D, Stieber J, Schätzlein A, Blume G. Ultraflexible vesicles, Transfersomes, have an extremely low pore penetration resistance and transport therapeutic amounts of insulin across the intact mammalian skin. *Biochimica et Biophysica Acta (BBA)-Biomembranes*. 1998 Jan 19;1368(2):201-15.
- 32) Halnor VV, Pande VV, Borawake DD, Nagare HS. Nanoemulsion: A novel platform for drug delivery system. *J Mat Sci Nanotechol*. 2018;6(1):104.
- 33) Ghanbarzadeh S, Arami S. Enhanced transdermal delivery of diclofenac sodium via conventional liposomes, ethosomes, and transfersomes. *Biomed research international*. 2013 Oct;2013.
- 34) Burgess DJ, Hickey AJ. Microsphere technology and applications. In: Swarbrick J, editor. *Encyclopedia of Pharmaceutical Technology*. 3rd ed. Vol.4. New York: Informa Healthcare; p. 2328-2338.
- 35) You J, Cui FD, Han X, Wang YS, Yang L, Yu YW, Li OP. Study of the preparation of sustained release microspheres containing zedoary turmeric oil by the emulsion solvent diffusion method and evaluation of the selfemulsification and bioavailability of the oil. *Colloids Surf B Biointerfaces*. 2006; 48(1): 35- 41.
- 36) Arora P, Mukherjee B. Design, development, physicochemical, and in vitro and in vivo evaluation of transdermal patches containing diclofenac diethylammonium salt. *Journal of pharmaceutical sciences*. 2002 Sep 1;91(9):2076-89.
- 37) Chaturvedi M, Kumar M, Sinhal A, Saifi A. Recent development in novel drug delivery systems of herbal drugs. *International Journal of Green Pharmacy (IJGP)*. 2011;5(2).