

Indonesian Journal of Pharmaceutical and Clinical Research Journal homepage: https://idipcr.usu.ac.id



Herbal Medicines and Recent Development on Novel Herbal Drug Delivery System

Aziz Ahmed^{*1}, Mohd Shuaib², Mrunal K. Shirsat³, Deeksha Sharma⁴

¹Professor and Researcher at Department of Pharmacy, Jaipur College of Pharmacy, Jaipur, Pin 302022, Rajasthan, India

² Professor and Researcher at Department of Pharmacy, Kalka Institute for Research & Advanced Studies, Meerut, Pin 250002, U.P, India

³ Principal, Professor and Researcher at Shri Balaji Shikshan Mandal, Pharmacy College, Ambajogai, Maharastra

⁴ Assistant Professor and Researcher at Department of Pharmacy, Jaipur College of Pharmacy, Jaipur, Pin 302022, Rajasthan, India

*Corresponding Author: ahmedaziz34@gmail.com

ARTICLE INFO Article history: Recieved : 1 january 2023 Revised : 2 March 2023 Accepted : 4 July 2023 Available online 8 august 2023

E-ISSN: 2620-3731 P-ISSN: 2615-6199

How to cite:

Ahmed A, Shuaib M, Shirsat MK, Sharma D. Herbal Medicines and Recent Development on Novel Herbal Drug Delivery System. Indonesian Journal of Pharmaceutical and Clinical Research. 2023 Jul 20;6(1):013-024.



ABSTRACT

The World Health Organization (WHO) defines herbal medicine as a technique that uses herbs, herbal ingredients, herbal preparations, and finished herbal products. Herbal remedies contain a variety of chemical components known as phytochemicals, which fall into a number of categories including saponins, flavonoids, glycosides, tannins, alkaloids, and terpenoids. Due to the presence of these phytochemicals, herbal medications can be used to treat a variety of ailments and diseases, including gastrointestinal problems, skin infections, arthritis, migraines, and weariness. Herbal medicines have less major adverse effects than conventional pharmaceuticals and are less expensive. New herbal formulations can include transfersomes, ethosomes, microspheres, phytosomes, liposomes, polymeric nanoparticles, and nanocapsules. In comparison to traditional herbal medicines, the novel herbal drug delivery systems offer many advantages, including increased solubility and bioavailability, protection from side effects, enhanced pharmacological action, increased stability, better delivery to tissue macrophages, consistent delivery, and protection against the physical and chemical breakdown of active ingredients. To incorporate standardised herbal extract or aqueously soluble active ingredients into phospholipids to build lipid companionable molecular complexes, phytosome has been described as a patented innovative herbal technology produced by a leading manufacturer of medicines and nutraceuticals. The use of herbal medicines can be expanded in order to increase their efficacy by incorporating them into more sophisticated medications. Keyword: Herbal medicines; phytochemical; Novel drug delivery system

ABSTRAK

Organisasi Kesehatan Dunia (WHO) mendefinisikan pengobatan herbal sebagai teknik pengobatan yang menggunakan jamu, bahan jamu, sediaan jamu, dan produk jamu jadi. Obat herbal mengandung berbagai komponen kimia yang dikenal sebagai fitokimia, yang termasuk dalam beberapa kategori termasuk saponin, flavonoid, glikosida, tanin, alkaloid, dan terpenoid. Karena adanya senyawa fitokimia ini, pengobatan herbal dapat digunakan untuk mengobati berbagai penyakit, termasuk masalah pencernaan, infeksi kulit, radang sendi, migrain, dan kelelahan. Obat-obatan herbal memiliki efek samping yang lebih kecil dan harga yang lebih terjangkau daripada obat-obatan konvensional. Formulasi herbal baru dapat mencakup transfersom, etosom, mikrosfer, fitosom, liposom, nanopartikel polimer, dan kapsul nano. Dibandingkan dengan obat herbal tradisional, sistem penghantaran obat herbal baru menawarkan banyak keuntungan, termasuk peningkatan kelarutan dan bioavailabilitas, penghantaran yang

lebih baik ke makrofag jaringan, penghantaran yang konsisten, dan perlindungan bahan aktif dari peruraian bahan kimia. Dalam pembuatan ekstrak herbal standar atau bahan aktif yang larut dalam air ke dalam fosfolipid untuk membangun molekul kompleks yang mengandung lipid, fitosom sebagai teknologi herbal inovatif telah dipatenkan dan diproduksi oleh produsen obat terkemuka. Penggunaan obat-obatan herbal dapat diperluas untuk meningkatkan khasiatnya dengan memformulasikannya ke dalam sistem penghantaran obat yang lebih canggih.

Kata Kunci: Obat herbal; fitokimia; Sistem penghantaran obat baru

1. Introduction

Herbal medicines (HMs) are the backbone of balancing and alternative treatments, which in modern times are gradually gaining worldwide recognition and gradually moving towards integration into healthcare systems [1]. The use of HMs has increased by gender, social class and race in developing countries of the world [2–7]. Due to the growing demand for HM in the global market (local and international), the annual revenue increase is about to reach 62 billion USD [8]. Important drivers of this expansion of investment and use include its low cost, widespread acceptance due to its position as a natural product with low toxicity, effectiveness for hard-to-identify diseases and versatility in convenience, preparation and use.

HM uses preparations from bioactive natural ingredients including herbs or botanicals, some formulations may include ingredients such as mushroom and bee products, as well as minerals (kaolin, bentonite), ash, seashells, insects and animal parts, and is used to protect health and manage various diseases. HM can provide many benefits, as well as some that may have unwanted effects. The pharmacological effects and most of the toxic effects caused by HM are related to the activity of secondary metabolites. In a number of cases, HM has been used correctly, abused and sometimes misunderstood. The benefits of HM in the medical field in general depend on accurate and complete information, and poor management experience and confusion have been created due to lack of information about herbal medicine, especially about their benefits and possible disadvantages of herbal medicines. key departments of healthcare: doctors, pharmacists, nurses and the community. The appeal of herbal medicine will continue to increase worldwide for a variety of reasons, so there is an urgent need for true and sufficient information about HM, especially those that highlight key topics such as Benefits, efficacy, safety, toxicity, research and development, formulation, regulation, analytical techniques, quality control, economic value, etc. [9]. Indeed, some HMs is associated with a number of important adverse actions related to cardiac, neurological, and nephrotoxicity as well as cancer [10–12]. HM toxicity can occur and their extent can vary depending on the herb or herbal ingredient, preparation and user, ranging from mild to severe and sometimes fatal. Counterfeiting and the combined use of herbal medicines with conventional drugs is an area that requires further awareness, thus requiring strict regulation, clarification and control.

A few years ago, there was a lot of awareness about the improvement of a new herbal medicine delivery system. The conventional dosage form as well as the unconvincing extended-release dosage form intends to bind the drug components together at a rate other than as required by the human body, during healing time, which assigns active ingredients to their preferred destination to achieve an extreme therapeutic response. In herbal formulation research, emerging nanoscale dosage forms (polymer nanoparticle and nanocapsule, liposomes, solid lipid nanoparticles, phytosomes and nanoemulsions) show a wide range of benefits to formulations. Herbs, as well as increase solubility and blood concentration, resist toxicity, develop pharmacological effects, improve stability, improve tissue macrophage distribution, distribution consistency and protect against physical and chemical degradation. Therefore, the nano-sized NDDS of herbal ingredients has the potential to increase the effect and eliminate the problems associated with herbal medicine [33].

2. Application of herbal medicine

Herbal medicine (HB) includes herbs, plant materials, herbal preparations and herbal finished products containing active ingredients that are plant parts, or ingredients. Other botanical materials, or combinations, and specially used for the prevention and treatment of diseases [13]. Today HM remains the mainstay of primary health care in many rural African and Asian communities. It is also a fundamental part of the culture of many societies around the world. Many herbs and herbal formulas have a long traditional history of folk uses and health benefits. Scientific research has revealed that HM contains complex chemical compounds responsible for their pharmacological effects, corresponding to their health benefits and/or

toxicity [1]. HMs has been used as prophylactic drugs to preserve passive health as well as to radically treat a variety of diseases from mild to severe [14-17]. Currently, HMs are formulated and used in many different forms, which also affects their performance. The dosage form of herbal medicine varies greatly depending on factors such as the form of the disease being treated, the route of application, the patient, the culture and even the philosophical background. In traditional medicine and clinics, HM is often prepared from fresh or dried herbs, often prepared in the form of infusions, decoction, poultice, powder to apply on open wounds or put in native drinks, puddings, etc. Conventional commercial HM products are generally available in pill, capsule, tablet, powder/granule, cream, ointment form, etc. Layout of HMs in Pharmaceutical dosage forms are said to improve dosing accuracy, aesthetics as well as compliance by inducing use. Safety and effectiveness is another important factor that governs the use and marketing of HM. The quality of herbal products really depends on the safety and effectiveness of the herbal ingredients in terms of the chemical ingredients inside, the type of contaminant as well as the manufacturing process. The chemical compounds present in herbal ingredients have shown many benefits in controlling many diseases, including complex diseases/conditions such as HIV/AIDS, cancer, sickle cell disease, malaria and other infectious as well as non-communicable diseases. Infectious Diseases like diabetes, obesity, infertility, etc. Although widely recognized, the benefits and sometimes misconceptions: there is an urgent need for critical HM management to ensure that complete and accurate information about herbal medicine and herbal products are available to healthcare providers in particular and the general public, particularly on topics such as the identification, quality, safety and effectiveness of HM.

3. Polyherbal Formulation

Compared to man-made pills that usually consist of mostly single chemical drugs (natural ingredients), HM is clearly made up of many compounds commonly found in extracts, in an unrefined state. Some of the complete natural dosing literature is held from conventional pills that are often associated with many natural pills as energy ingredients [18]. The unique formation forms of maximal HMs may be the reason used for the majority of their earnings [14, 19]. The factorial polynomial components of some HMs, as shown in some people's recipes, are often crucial to the overall product if desired results are to be produced. Multi-ingredients can also enhance earnings by concurrent use of enhanced precise pharmacological activities as well as absorption, distribution, metabolism and elimination of bioactive ingredients. In addition, some factors may also continue on multiple receptors or physiological structures: this is probably why many HMs exhibit a wide range of therapeutic benefits.

3. Efficacy of Herbal Medicine

HM is applied for treatment, pain relief, cure and prevention of diseases, especially typical diseases in limited herbal environments [14, 16, and 20]. There are many lines of herbs with health promotion/treatment claims, although rarer varieties have clinical or proven effectiveness. All of the motions in HM benefits and toxicity are related to the active ingredients. The growing interest in HM has also recommended further research in this area, which leads to more important facts as long as effectiveness and people's claims are alarmed. Various research efforts have supported the claims regarding the marketing of many natural products and nominated them as leaders in pharmaceutical drug fortification. However, many local HMs remain untested and their earnings are not verified. Inadequate facts about this item have made the truth about the healing benefits and aspect results very limited, raising doubts about their fitness income. It is also normal for many people to use HM along with pharmaceutical drugs and for a lot of information about HM about the possible end results of this exercise is not available as no studies have been done yet. Therefore, there may be a request for data regarding the possible outcomes of a combination of multiple HMs and commonly used traditional drugs. These facts must be generated by the research and improvement segment of all marketed HMs and are required by regulation. These contact information must also be disclosed in the package insert.

5. Secondary metabolites in herbal medicine

The pharmacological effects of HM are reliable for their maximum benefit and toxicity. These biological activities are mainly due to the existence of active complex chemical entities: secondary metabolites [21, 22]. Although some are responsible for the unique dynamic movements, others act as adaptive buffers and modulate the pharmacological movements generated by energy additives to make them much less toxic. This is probably why many herbal extracts or recipes will not be shaped by the remotely

refined chemical composition of the herb or recipe [23]. A complex class of compounds elicits a wide variety of actions in human and animal regimes and cellular cultures.

6. Health benefits of herbal medicine

Unlike standard drug treatments, the warning signs of HM people are diverse, hired to treat a wide variety of ailments [26]. Warning signs range from easy exercise situations like cold, pain, ground trauma to extreme situations like mental disorders, diabetes, malaria, sickle cell disease, tuberculosis, cancer, hypertension, infertility, etc. In some communities, HM is the primary aspect of health care number one. Indeed, no less than 80% of the agricultural population in Africa uses purely conventional, nature-based drug treatments for most of their healthcare. In Ghana, Mali, Nigeria, and Zambia, the number one treatment for 60% of children with superinfection due to malaria and other diseases is HM, which can be routinely given to patients. Rural South Africa also has a strong traditional medicine lifestyle, which depends on the HM. In China and India, HM owes money for about 50% of full fitness product usage. With the growing interest in HM worldwide, the list of medicinal herbs and products is growing, and the price to use is also increasing, even as traditional healthcare has to be available and easily accessible. Furthermore, in the United States, about 40% of the adult population has adopted natural medicines [27]. HM sales in Canada [28], Australia [6], and Europe, mainly Germany and France, are growing rapidly [29].

7. Reasons for improving the use of herbal medicine (HM)

Most reasons can be given for this:

A. Personal preference for HM

The usefulness of HM is a colossal temporal subculture embedded in the subcultures of many societies. In ancient times, people trusted him as a leading healthcare provider with great success. Despite the modernization and spread of traditional health care based on the use of pharmaceuticals. However, some people, especially in Africa and Asia, still endow HM with unique abilities: this human organization will unceasingly prioritize HM as their first aid source in every institution. viable societies regardless of their economic, academic, and social status.

B. Safety Awareness

In general, many ordinary consumers are of the opinion that HM is safe and does not pose any danger or effect on appearance. Although HMs are herbal products made up of plant materials, minerals, and some animal ingredients, jet, many HMs are certainly not without negative effects. While it is true that many HMs are much easier to tolerate than pharmaceutical pills, especially when used long-term to manage chronic diseases [30, 31]. Studies have shown that in some countries, including South Africa and Ghana, herbalists outnumber traditional physicians, while in India, China, and Vietnam, the number of herbalists is far out. Traditional herbalists and doctors are equivalent.

C. Easy access to HM

Especially in rural African and Asian groups where access to standard scientific services is both luxurious and sophisticated, a simple, reliable approach to healthcare The easiest and fastest are the Doctors of Science (TMP) whose treatment often depends on the HM. However, in societies where drugs are tightly regulated, HM is the result that is easily obtained at low cost and without a prescription.

D. Low-cost HM

In some rural communes, the rate of HM is often low compared to treatment with traditional medicines. The TMPs that provide services are often those in the network who frequently stay in the community with their clients (patients), due to the long travel distances to traditional clinical centers. Most HMs are organized in a way that improvises or natural substances are targeted at the person involved with an oral lesson on how to put them together and use them. Payment terms are often more flexible as TMP can also match component bills or payment types with content including clothing, chickens, goats, and more. This is despite the fact that in the version with natural products exclusively from abroad, the cost is often as high as traditional drugs and so on.

E. Efficacy in Treatment of Diseases with HM

At its peak, research activities to verify claims and determine high handling and protection requirements for natural substances and goods have increased go up. The protection and effectiveness of some natural products have been scientifically evaluated to verify the claims. Clinical evidence of protection and effectiveness has contributed to the development of assurance and recognition of many natural products. There are also some diseases in which patients have an indication to choose HM over medication [32].

8. Novel or Advanced approach of delivery system for herbal medicines

Since time immemorial, care has been taken to suggest to the physician the type of medicine most suitable for the patient so that the improvement of symptoms is more rapid and complete. Drugs, among other ingredients, protect, efficacy, and suitability, and the final product is usually recognized as a dosage form or drug delivery system. With the growth of all areas of science and technology, dosage forms have evolved from simple tablets and pills to particularly complex technological and centralized drug delivery systems known as NDDS [34]. In recent years, much interest has been focused on the development of his NDDS of plant constituents [35]. Herbal medicines are gaining popularity in the current medical field as they are keen to reduce toxic effects and enhance curative effects to treat various ailments. Some limitations, such as instability at highly acidic pH and liver metabolism, can lead to sub-therapeutic drug levels in the blood, leading to poor results.

Inclusion of novel herbal drug delivery technology reduces the drug decomposition and severe unwanted effects by addition of drugs to the no targeted areas and enhances the relieve of administration in the children and elder people [36]. Conventional dosage forms, with extended discharge dosage forms, are not proficient to accomplish the perfect necessities of novel carriers for instance capacity to bring the drug at a rate according to the need of the body and to convey the active components of herbal extract to the target area. For excellent blood level, crude herbal components must include a better balance between hydrophilicity (for dissolving into the intestinal fluids) and lipophilicity (to transfer the plasma layer). A lot of active components for instance phenolic compounds have fine aqueous solubility but are weakly absorbed in the intestine [37]. Because of their several ring large sized molecules which cannot be transferred by simple diffusion or their low solubility with oil and other lipids, harshly reducing their control to enter across the plasma membranes of the small intestine [38]. Therefore, the nano dimension NDDSs of plant components have a possible opportunity for increasing the natural development and devastating troubles connected with plant dosage forms [35]. Novel herbal drug delivery systems treat ailments by targeting just the affected part within a body and transferring the drug to that area. NDDS is helpful in supporting the plant drug at a determined rate and release of drug at the target area which lowers the harmful actions with an improvement in blood level of herbal components. In an herbal NDDS, the arrangement of the distribution of the herbal components is received by which the herbal component in carrier arrangement or in altering the social organization of the plant component at the molecular element. The assimilation of botanical components into delivery systems leads to improved solubility, safety from toxic effects, greater pharmacological efficacy, superior tissue macrophage delivery, consistent delivery, and protection from physical and chemical degradation. In addition, liposomes are also useful for delivering anti-tumor compounds by increasing the amount of plant in the target area and reducing the release or loading of the plant in normal cells/tissues, thereby blocking toxic effects in tissues. Phytosomes are calculated to properly release botanicals, such as ginseng (Ginkgo biloba) and readily bind phosphatidylcholine and botanical extracts.

9. Various forms of new technology for the delivery of herbal medicines

Many applications of new herbal medicine delivery systems involve various forms of technology are following:

A. Advanced Orally Dissolving Tablets

Ahsoka Life Sciences Limited produced Res Q, the world's first orally dissolving polyherbal tablet, an oral medicine that dissolves rapidly in the mouth. A new drug delivery system with enhanced efficacy. Ayurveda, an alternative medicine system, is an early attempt to prescribe dosage forms better suited for treating chronic diseases. Res Q is a dosage form containing multiple active ingredient extracts and is highly suitable for respiratory diseases and other pulmonary diseases such as asthma. This melt-in-the-mouth drug

delivery system ensures that the drug enters the blood directly, bypassing first-pass metabolism. It dissolves when mixed with saliva and absorbed in the mouth. This Res Q helps treat lung infections within 15 minutes. Thus, this product closely resembles the efficacy of sorbitrate, the newest drug that melts in the mouth and is used for heart disease [39].

B. Herbal Medicines and Controlled Release Formulations

Copyright Notice of Oral Medicines For Limited Release or Permanent Storage ff Granular Botanicals.

Granular botanicals and carriers release drug 4-18 hours after application of 75% of active ingredient. Active ingredients are selected from the hypericin, hyperforin, and echinacoside collections. This innovation has resulted in better herbal medicines, whose formulations suggest appropriate oral dosage forms of botanicals to provide the most favorable blood levels of biologically active ingredients and bring uniformity to the consumer. brings Oral dosage form with limited and stable release of Plantis in a matrix-engineered drug. B. Matrix tablets or microcapsules are two-piece capsules designated for drug delivery systems that ensure the normal transport of active ingredients over a period of time [40].

A complementary US copyright innovation is a sustained herbal dosage form in the form of sustained release microgranules containing *Ginkgo biloba* extract and its manufacturing process. Herbal extracts have reduced flowability and compressibility. Therefore, it is difficult for these herbal extracts to be included in various sustained-release tablets because a uniform amount of herbal extract with medicinal additives is required throughout the compression time. Microparticles can be formed by various techniques such as extrusion spheronization, fluidized airbed method, or cutting pan method. Extrusion-spheronization is suitable for high-potency pellets but requires more equipment. For manufacturing innovation granules, the cutting pan method is preferred because of its simple equipment and processes [41].

C. Liposomes as novel herbal formulations

These are micro-sized colloidal carriers, typically $0.05-5.0 \mu m$ in diameter, that are impulsively assembled during the migration of certain lipids into aqueous media [42]. These are round molecules that cover part of the solution and are free to move or drift through it. They can assume single, multiple, or many concentric layers. They are composed of aqueous lipids measured by maintaining lipophilic and hydrophilic collections of the same molecule. Upon binding with water, aqueous lipids transform into self-assembled colloidal molecules [35]. These novel formulations suggest potency to enhance the curative potential of antineoplastic agents by either increasing the amount of drug within cancer cells or decreasing its release in general tissues [43]. The main advantages of using liposomes are: (i) improved bioavailability, (ii) formulation acceptability, (iii) compound adaptability to allow for hydrophilic, amphiphilic, and lipophilic moieties, and (iv) The ease of altering its pharmacokinetic properties by variables andactive component.



Figure 1. Active constituents from herbal drugs employed in liposome novel herbal drug delivery system

D. Phytosome

Most of the active ingredients in herbal medicines are flavonoids, and their blood levels decrease when taken orally. Water-soluble active ingredients (mainly polyphenols) can be transformed into lipidcompatible molecular complexes known as phytosomes. These are more stable to escape the lipophilic plasma membrane and ultimately reach target organs, resulting in higher blood levels compared to simple plant extracts. Hydrophobic compounds that help create a balanced lipid active ingredient are soy-derived lipid-phospholipids, primarily phosphatidylcholines [44].



Figure 2. Utilization of herbal medicine in phytosome novel herbal drug delivery system

E. Nanomolecules

Nanomolecules are well-organized herbal preparations to release both hydrophilic and hydrophobic compounds. Nanoparticles are nano-sized components from 10 to 1000 mm [45]. The primary purpose of forming nanomolecules as a release protocol is to control particle dimensions, surface properties, and release of biochemical components to target-specifically deliver drugs at the most therapeutically advantageous rates and dosing regimens [48]. In recent years, recyclable polymeric nanomolecules have been used in significant concentrations as a viable drug delivery strategy [47]. It is a dispersed structure in a nanocapsule containing a polymer layer and a core of active ingredients. Nanoization has many benefits compared to individual herbal formulations, including increased dissolution of ingredients, soaking of therapeutic doses, and improved absorption of active ingredients [46].



Figure 3. Some important active constituents from herbal drugs employed in nanoherbal herbal drug delivery system

F. Niosomes as novel formulations of herbal medicines

Niosomes are multiple unilamellar sacs composed of alkyl or dialkyl polyglycerol ether groups and nonionized surfactants of cholesterol. Previous studies involving L'Oreal have shown that niosomes have common properties as potent drug carriers similar to those of liposomes [49]. They differ from liposomes in one respect. Liposomes have problems such as being expensive, being unstable due to the oxidative degradation of phospholipids and other components, requiring special treatment, and not matching the purity of natural phospholipids. Niosomes do not contain these problems [50].

G. Proniosome

These novel formulations are superior to niosomes and can be used in a variety of applications to deliver active ingredients to preferred target areas [51]. These formulations interact with moisture from the skin and niosomes [48]. These are surfactant-encapsulated water-soluble carrier components that can be converted to niosome dispersions in warm aqueous media by gentle agitation immediately prior to exposure [52].



Figure 4. Proniosome herbal drug delivery system and their

H. Transdermal Drug Delivery Systems for Herbal Ingredients

This novel delivery system is enhanced for penetration of ingredients through the skin to limit therapeutic efficacy on diseased skin (local delivery) and for palliative and systemic drug delivery [54].

However, they have not achieved this potential feat with other drugs [34]. This system offers the advantages of controlled drug release, better drug levels, reduced adverse effects, and ease of use. The design of transdermal films containing botanical ingredients such as *Boswellia serrata* and curcumin (*Curcuma longa*) is more suitable for delivering herbal medicines through this delivery system, which uses the skin as the target area for stable drug release into the bloodstream. Good try. Therefore, this new system goes through first-pass metabolism of herbal ingredients without the irritation associated with injection. Moreover, this system prolongs drug release at extraordinary doses by zero-order kinetics, and this method is readily available. The use of turmeric in this new system for the local effect of ingredients in targeted areas of drug release can also be described as the latest indication of the Ayurvedic turmeric pack or jump [55].

I. Microspheres as novel delivery systems

These are discrete round particles with typical particle sizes ranging from 1 to 50 microns [55]. These drug delivery systems are consistent in protecting drug components in target areas with specific actions to maintain preferred amounts of drug in conditions of concern without adverse effects. Considered and accepted. This is a supportive method that significantly prolongs the duration of action of drug components and increases patient satisfaction. Stable blood levels are ensured, thus minimizing total drug dosage and minor side effects [56]. To date, many active ingredients in herbal medicines such as rutin, camptothecin, cedar oil, tetrandrine, and quercetin have been transformed into microspheres. Information on trapped microspheres and magnetic microspheres has also become widely available in recent years. Immunomicrospheres retain immunity as an effect of antibodies and antigens are encapsulated or adsorbed onto polymer microspheres [57].



Figure 5. Role of herbal microsphere in various disease and disorders

J. Emulsion as a new drug delivery system

Emulsions consist of two insoluble liquids, one in the form of droplets inside the other [58]. Emulsions are usually mixtures of an oil phase, an aqueous phase, surfactants, and subsurfactants. Its form is a translucent to transparent liquid. These can be classified into normal emulsion (0.1-100 μ m), micro-emulsion (10-100 nm), sub-micro-emulsion (100-600 nm), etc. Microemulsions are also known as nanoemulsions and submicroemulsions are also identified as lipid emulsions. The emulsion distributes to the site of action in vivo due to magnetism for lymph. In addition, since the drug is in the internal phase and is in direct contact with bodily and tissue fluids, it can be delivered stably for a long time [59].

K. Ethosomes as a new drug delivery system

Recent advances in patch technology have produced this novel delivery system consisting of an ethosome drug moiety. These systems contain soy phosphatidylcholine, ethanol, and water. They produce multilamellar vesicles and enhance their trapping capacity for various lipophilic types of particles. Flexible vesicles and transfersomes have also been used as drug carriers for a variety of small molecules, peptides,

proteins, and vaccines [60]. They have enhanced deformability and entrapment efficiency, fully penetrate the skin, and are able to penetrate the skin. can improve drug release from Like other liposomes, the properties of ethosomes allow the legitimate transfer of drugs through the stratum corneum into deeper layers of the skin, or even into the systemic circulation [61]. Very important as a delivery system. In addition, ethosome transporters can also propose well-organized intracellular release of both hydrophilic and lipophilic drugs [62]. Enhanced percutaneous absorption of matrine, an anti-inflammatory herbal drug, enters the fibrocytes [64].

L. Transpherosomes

These are specially optimized debris or vesicles that are able to counteract external stress through short-lived and energetically favorable transformations [65]. A boom in new strategies involving transfersomes is It has helped overcome the catastrophe caused by drug delivery, which currently cannot successfully deliver larger molecules and diffusion across the stratum corneum is a paying step. These elastic vesicles can pass through pores and pores of the skin and can carry large molecules that are many times smaller than their own length [66; 67].

10. Conclusion:

Herbal medicine requires a systematic approach to manufacture components in novel ways to increase patient compliance and avoid frequent dosing. This can be completed by manufacturing new drug delivery systems for active ingredients in herbal medicines. New drug delivery systems not only minimize frequent dosing and overcome non-compliance but also help increase drug pricing, including reducing toxicity and increasing bioavailability. Recently, researchers have shifted their focus to developing drug delivery systems for herbal medicines using scientific approaches. A new approach can also help you conquer and stay in the market. However, there are many limitations and problems in herbal medicine that need to be resolved, such as the use of herbal medicine, the invention of various animal models for toxicity and safety evaluation, and legal and regulatory aspects of herbal medicine.

Conflict of Interest

Authors declare no conflicts of interest

References

- [1] Bent S. Herbal medicine in the United States: Review of efficacy, safety, and regulation. *J Gen Intern Med* 2008; **23**(6):854-859.
- [2] Kessler RC, Davis RB, Foster DF, Van Rompay MI, Walters EE, Wilkey SA, et al. Long-term trends in the use of complementary and alternative medical therapies in the United States. *Ann Intern Med* 2001;**135**(4):262-268.
- [3] Bodeker G, Burford G. Traditional, complementary and alternative medicine: Policy and public health perspectives. *Bull World Health Organ* 2007;**86**(1):77-78.
- [4] Fasinu PS, Bouic PJ, Rosenkranz B. An overview of the evidence and mechanisms of herb– drug interactions. *Front Pharmacol* 2012; **3**: 69. doi: 10.3389/fphar.2012.00069
- [5] Bensoussan A, Myers SP, Wu S, O'Connor K. Naturopathic and western herbal medicine practice in Australia: A workforce survey. *Complement Ther Med* 2004;**12**(1):17-27.
- [6] Van-Wyk BE, deWet H, Van-Heerden FR. An ethnobotanical survey of medicinal plants in the southeastern Karoo, South Africa. *S Afr J Bot* 2008;**74**:696-704.
- [7] WHO. Traditional Medicine Strategy 2002-2005. Geneva: WHO. p. 2002
- [8] Barrett B, Kiefer D, Rabago D. Assessing the risks and benefits of herbal medicine: An overview of scientific evidence. *Altern Ther Health Med* 1999;**5**: 40-49
- [9] Nortier JL, Martinez MC, Schmeiser HH, et al. Urothelial carcinoma associated with the use of a Chinese herb (Aristolochia fangchi). *N Engl J Med* 2000; **342**:1686-1692.
- [10] Stickel F, Patsenker E, Schuppan D. Herbal hepatotoxicity. J Hepatol 2005; 43:901-910.
- [11] Haller CA, Benowitz NL. Adverse cardiovascular and central nervous system events associated with dietary supplements containing ephedra alkaloids. *N Engl J Med* 2000; **343**:1833-1838.
- [12] WHO. General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine. Vol. 13. Geneva: World Health Organization; 2000.

- [13] Shinde VM, Dhalwal K, Potdar M, Mahadik KR. Application of quality control principles to herbal drugs. *Int J Phytomedicine* 2009; 4-8.
- [14] Mosihuzzaman M. Herbal medicine in healthcare—an overview. Nat Prod Commun 2012;7(6):807-812.
- [15] Coleman LM, Fowler LL, Williams ME. Use of unproven therapies by people with Alzheimer's disease. J Am Geriatr Soc 1995;43:747-750.
- [16] Ansari FZ, Alam S, Jain P, Akhter S, Ansari MZH. Vitiligo and its herbal treatment. *Pharmacol Rev* 2008;**12**:137-113.
- [17] Parasuraman U, Thing GS, So DA. Polyherbal formulation: Concept of Ayurveda. *Pharmacogn Rev* 2014;**8**(16):73-80.
- [18] Spinella M. The importance of pharmacological synergy in psychoactive herbal medicines. Altern Med Rev 2002;7:130-137.
- [19] Mahima RA, Deb R, Latheef SK, Abdul Samad H, Tiwari R, Verma AK, et al. Immunomodulatory and therapeutic potentials of herbal, traditional/indigenous and ethnoveterinary medicines. *Pak J Biol Sci* 2012;**15**:754-774.
- [20] Akhtar N, Ali M, Alam MS. Herbal drugs used in dental care. *Pharm Rev* 2005; 10:61-68.
- [21] Seigler DS. *Plant Secondary Metabolism*. New York: Springer Science Business Media; 1995. doi: 10.1007/978-1-4615-4913-0
- [22] Delgoda R, Murray JE. Evolutionary perspectives on the role of plant secondary metabolites. In: Badal S, Delgoda R, editors. *Pharmacognosy: Fundamentals, Applications and Strategies*. 1st ed. Oxoford, UK: Academic Press; 2017. p. 93-100.
- [23] Wink M. Modes of action of herbal medicines and plant secondary metabolites. *Medicine*. 2015; 2:251-286.
- [24] Harborne JB, Baxter H. *Phytochemical Dictionary—A Handbook of Bioactive Compounds from Plants*. London, UK: Taylor and Francis; 1993.
- [25] Wink M. Functions of plant secondary metabolites and their exploitation in biotechnology. In: *Annual Plant Reviews*. Vol. 39. London, UK: Wiley-Blackwell; 2010.
- [26] Ernst E. The efficacy of herbal medicine—an overview. Fundam Clin Pharmacol 2005; 19(4):405-409.
- [27] Tachjian A, Maria V, Jahangir A. Use of herbal products and potential interactions in patients with patient cardiovascular disease. *J Am Coll Cardiol* 2010; **55**(6):515-525.
- [28] Calixto J. Efficacy, safety, quality control, marketing and regulatory guidelines for herbal medicines (phytotherapeutic agents). *Braz J Med Biol* 2000; **33**:179-189.
- [29] Capasso R, Borrelli F, Aviello G, Mascolo N, Romano B. Phytotherapy and quality of herbal medicines. *Fitoterapia* 2000; **71**(1):58-65.
- [30] Ekor M. The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. *Front Pharmacol* 2013; **4**:177.
- [31] Firenzuoli F, Gori L. Herbal medicine today: Clinical and research issues. eCAM. 2007; 4(S1):37-40.
- [32] Tavakoli J, Miar S, Zadehzare MM, Akbari H. Evaluation of effectiveness of herbal medication in cancer care: A review study. *Iran J Cancer Prev* 2012; **5**(3):144-156.
- [33] Medina OP, Zhu Y, Kairemo K. Targeted liposomal drug delivery in cancer. *Curr Pharm Des* 2004; **10**:2981-9.
- [34] Mandal SC, Mandal M. Current status and future prospects of new drug delivery system. *Pharm Times* 2010; 42:13-6.
- [35] Ajazuddin SS. Applications of novel drug delivery system for herbal formulations. *Fitoterapia* 2010; 81:680-9.
- [36] Goyal A, Kumar S, Nagpal M, Singh I, Arora S. Potential of novel drug delivery systems for herbal drugs. *Indian J Pharm Educ Res* 2011; **45**:225-35.
- [37] Manach C, Scalbert A, Morand C, Rémésy C, Jiménez L. Polyphenols: Food sources and bioavailability. *Am J Clin Nutr* 2004; **79**:727-47.
- [38] Chauhan NS, Rajan G, Gopalakrishna B. Phytosomes: A potential phyto-phospholipid carriers for herbal drug delivery. *J Pharm Res* 2009; **2**:1267-70.
- [39] Parakh SR, Gothoskar AV. Review of mouth dissolving tablet technologies. Pharmaceutical Technology. Duluth, MN: *Advanstar Communications*; 2003. p. 47-52.
- [40] Blatt Y, Kimmelman E, Cohen D, Rotman A. *Microencapsulated and controlled-release herbal formulations*. United States Patent; 2002.
- [41] Marechal D, Yang Wg, Yuzhang H. Sustained-release microgranules containing Ginkgo biloba extract and the process for manufacturing these. United States Patent; 2009. p.7569236.

- [42] Sterer N, Nuas S, Mizrahi B, Goldenberg C, Weiss EI, Domb A, et al. Oral malodor reduction by a palatal mucoadhesive tablet containing herbal formulation. *J Dent* 2008; **36**:535-9.
- [43] Sharma A, Sharma US. Liposomes in drug delivery: Progress and limitations. *Int J Pharm* 1997; **154**:123-40.
- [44] Zhong H, DengY, Wang X, YangB. Multivesicular liposome formulation for the sustained delivery of breviscapine. *Int J Pharm* 2005; 301:15-24.
- [45] Youfang C, Xianfu L, Hyunjin P, Richard G. Evaluation of artemisnin nanoparticles. *Nanomed Nanotechnol Biol Med* 2009; **5**:316-22.
- [46] Brigger I, Dubernet C, Couvreur P. Nanoparticles in cancer therapy and diagnosis. *Adv Drug Deliv Rev* 2002; **54**:631-51.
- [47] Mei Z, Chen H, Weng T, Yang Y, Yang X. Solid lipid nanoparticle and microemulsion for topical delivery of triptolide. *Eur J Pharm Biopharm* 2003; **56**:189-96.
- [48] Mohanraj VJ, Chen Y. Nanoparticles: A review. Trop J Pharm Res 2006; 5:561-73.
- [49] Tangri P, Khurana S. Niosomes: Formulation and evaluation. Int J Biopharm 2011; 2:47-53.
- [50] Gupta S, Singh RP, Lokwani P, Yadav S, Gupta SK. Vesicular system as targeted drug delivery system: An overview. *Int J Pharm Technol* 2011;**3**:987-1021.
- [51] Shukla ND, Tiwari M. Proniosomal drug delivery systems Clinical applications. Int J Res Pharm Biomed Sci 2011; 2:880-7.
- [52] Raja K, Ukken JP, Athul PV, Tamizharasi S, Sivakumar T. Formulation and evaluation of maltodextrin based proniosomal drug delivery system containing anti-diabetic (glipizide) drug. *Int J Pharm Technol Res* 2011; 3:471-7.
- [53] Yasam VR, Jakki SL, Natarajan J, Kuppusamy G. A review on novel vesicular drug delivery: Proniosomes. *Drug Deliv* 2014; **21**:243-9.
- [54] Garala KC, Shinde AJ, Shah PH. Formulation and in vitro characterization of monolithic matrix transdermal systems using hpmc/ eudragit s 100 polymer blends. *Int J Pharm Pharm Sci* 2009; **1**:108-20.
- [55] Verma M, Gupta PK, Varsha BP, Purohit AP. Development of transdermal drug dosage formulation for the anti-rheumatic ayurvedic medicinal plants. *Anc Sci Life* 2007; **11**:66-9.
- [56] Meena KP, Dangi JS, Samal PK, Namdeo KP. Recent advances in microspheres manufacturing technology. *Int J Pharm Technol* 2011; **3**:854-93.
- [57] Lakshmana PS, Shirwaikar AA, Shirwaikar A, Kumar A. Formulation and evaluation of sustained release microspheres of rosin containing aceclofenac. *Ars Pharm* 2009; **50**:51-62.
- [58] Gavini E, Alamanni MC, Cossu M, Giunchedi P. Tabletted microspheres containing Cynara scolymus (var. spinoso sardo) extract for the preparation of controlled release nutraceutical matrices. J Microencapsul 2005; 22:487-99.
- [59] Kun Z, Caigang L, Zhuo Z, Lijuan Z. The effect of elemene on lung adenocarcinoma A549 cell radiosensitivity and elucidation of its mechanism. *Clinics* 2015;70:556–62. doi: 10.6061/clinics/2015(08)05
- [60] Song YM, Ping QN, Wu ZH. Preparation of silybin nano emulsion and its pharmacokinetics in rabbits. J Chin Pharm Univ 2005; 5:427-31.
- [61] Vicentini FT, Simi TR, Del Ciampo JO, Wolga NO, Pitol DL, Iyomasa MM, et al. Quercetin in w/o microemulsion: In vitro and in vivo skin penetration and efficacy against UVB-induced skin damages evaluated in vivo. *Eur J Pharm Biopharm* 2008;**69**:948-57.
- [62] Aggarwal G, Garg A, Dhawan S. Transdermal drug delivery: Evolving technologies and expanding opportunities. *Indian J Pharm Educ Res* 2009;**43**:251-9.
- [63] Dayan N, Touitou E. Carriers for skin delivery of trihexyphenidyl HCl: Ethosomes vs. liposomes. *Biomaterials* 2000; **21**:1879-85.
- [64] Touitou E, Godin B, Dayan N, Weiss C, Piliponsky A, Levi-Schaffer F, et al. Intracellular delivery mediated by an ethosomal carrier. *Biomaterials* 2001; **22**:3053-9.
- [65] Abdulbaqi IM, Darwis Y, Khan NA, Assi RA, Khan AA. Ethosomal nanocarriers: The impact of constituents and formulation techniques on ethosomal properties, in vivo studies, and clinical trials. *Int J Nanomedicine* 2016;11:2279-304.
- [66] Walve JR, Bakliwal SR, Rane BR, Pawar SP. Transfersomes: A surrogated carrier for transdermal drug delivery system. *Int J Appl Biol Pharm Technol* 2011; **2**:204-13.
- [67] Pinto JF. Site-specific drug delivery systems within the gastro-intestinal tract: From the mouth to the colon. *Int J Pharm* 2010; **395**:44-52.