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Traditional Herbal Medicines: Macro Dosages Forms to Nanoformulations

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Abstract

Traditional herbal medicines are used to combat various ailments throughout the world. They are used as therapeutics in developing countries, while as a complementary or alternative treatments in many developed countries. In spite of their extraordinary potential and excellent *in vitro* activities, many herbal drugs and natural products have limited therapeutic actions on oral administration. Novel drug delivery systems with the application of various nanotechnology tools can solve the problems associated with solubility, instability and bioavailability of herbal medicines and natural products. In this minireview, limitations with traditional herbal medicines for oral administration and ways to improve their bioavailability and bioactivity have been briefly described.

Background

Medicinal plants or herbs have been used since the dawn of civilization as a remedy for various ailments. The utilization of medicinal plants is very important in many rural communities around the globe as majority of populations in some Asian and African countries rely on herbal traditional medicine to fulfill their primary health care needs [1].

Medicinal plants are rich sources of drugs, nutraceuticals, food supplements, cosmetics and pharmaceuticals. In recent years, due to side effects of synthetic drugs, natural products are gaining popularity in the world market. The increasing demand of herbal products is due to their recognition as non-toxic, having less side effects, better compatibility and availability at affordable prices [2-4]. There is gaining popularity of herbal medicine in developed countries, particularly for chronic diseases. Nearly 70% of clinicians in France and Germany regularly prescribe herbal medicine and more than 50% of the population in developed countries has used herbal medications at least once in life [5-6].

Oriental medical systems such as traditional Chinese medicine and Ayurveda believe in maintaining, harmonizing and restoring balance between nature and human beings while treating patients. The holistic and systematic ideology of oriental medicine differs from the reductionist or mechanistic approach of Western medicine regarding human health and disease management. As medical treatment is gradually moving towards multidrug therapy with the emphasis on protective, repair and immunostimulatory mechanisms of the human body, traditional medicine has great potential in the years to come [7]. In general, the oriental medical formulations consist of medicinal plants and their formulations in the form of powder, pills, tablets, infusions, syrups, lotions, pastes etc. that contain pharmacologically active ingredients. Most of these are administered through oral route as it is more acceptable and preferred one. Oriental medical systems believe that poly-herbalism or synergism of multi-components achieve greater therapeutic efficacy, which is much relevant in treating complex diseases [8,9]. It is believed that the primary ingredient in the formulation acts as principal therapeutic agent, the minor ones enhance the activity of major one and remaining components either reduce the toxicity, enhance drug delivery to specific site or exert a harmonizing effects [9]. Interestingly not only in traditional medicine, recent scientific findings also reveal that the separation and purification of the crude extracts lead to the partial or full loss of the pharmacological properties of the crude extracts [10].

Despite their huge potential, there is limitation with some traditional drugs and natural products on oral delivery due to their poor solubility and absorption that prevent desired clinical effects [11-14]. Several plant extracts and isolated compounds revealing excellent *in vitro* activities are not effective *in vivo*. Various secondary plant metabolites like polyphenols exhibit remarkable *in vitro* pharmacological properties such as antiaging, antiallergenic, antiinflammatory, antimicrobial, antioxidant, cardioprotective, etc. Unfortunately, their instability and low bioavailability reduce their effectiveness to great extent when taken orally in traditional dose forms. Interestingly, encapsulation of polyphenols using nanotechnology significantly improves their stability and bioavailability both *in vitro* and *in vivo* [15].

Effective and sustained target delivery of the herbal drug is important to increase patient adherence and prevent repetitive

administration [16]. Moreover, efficacy of herbal drugs and their formulations depend on the bioavailability of active constituents to the target sites. Suitable carriers and formulations along with proper administration is needed for successful delivery and optimum effectiveness of herbals and their active constituents. Hence, integration of the nanocarriers as drug delivery systems of the traditional medicine is essential to battle chronic diseases such as diabetes, cancer and others [13] as these delivery systems can instantly release the target drug in the biological fluids in free form.

To overcome the limitations of conventional methods, development of novel herbal drug delivery systems such as nano emulsions, micro/nano spheres, liposomes, transfersomes, phytosomes, dendrimers, nanoparticles is utmost important to:

a. Increase their solubility, bioavailability and pharmacological activities,

b. Reduce toxicity,

c. Improve sustained delivery,

d. Improve stability and

e. protect from degradation [11, 14, 16-19].

Additionally, novel drug delivery systems improve the taste, color, flavor, texture, and consistency of the natural ingredients [20].

Among above delivery systems, liposome seems more promising one; not only for its encapsulation efficiency of hydrophilic, amphiphilic and hydrophobic drugs but also due to its biocompatibility, biodegradability and drug loading efficiency [21]. Tiny particles below cell size promote higher absorption and particle uptake, by enhancing the mechanisms of passive transport through the intestinal membranes and reach specific targets more easily than bulky drugs [12, 22].

The majority of the bioactive agents from medicinal plants are either poorly soluble or lipophilic [23]. Their poor solubility in gastrointestinal tract, leads to poor absorption and ultimately poor bioavailability [14]. However, their nanoformulations enable to prevent such barriers. Nanoformulation of *Cuscuta chinensis* extract showed better antioxidant and hepatoprotective effects than crude extract [24]. Poly-ε-caprolactone nanoparticles containing an aqueous seed extract of *Syzygium cumini* reveal high protection against ox-LDL and superior anti-candida activity, [25]. Similarly, polymeric microspheres encapsulating infusion of *Woodfordia fruticosa* flowers were prepared [26] to improve the solubility, stability and bioavailability of its bioactive constituents and nano gold particles from the plant were effective in preventing microbial adhesion and wound healing [27]. Herbal drugs encapsulated in polymer nanoparticles were highly effective than their conventional forms in treating osteoporosis [28]. Moreover, polymeric nanospheres of *Ginkgo biloba* extracts exhibited a better sustained release than crude extract in artificial gastric and intestinal juices [29].

Hydrophobicity of many bioactive compounds severely reduce their oral administration effectiveness. Resveratrol and quercetin shows poor activity *in vivo* due to the poor solubility in their bulky form. However, their solubility is improved 40- and 650-fold respectively after the development of appropriate nanoformulations [30]. Curcumin, another bioactive natural product and a promising candidate against many diseases including cancer has limitations due to its poor bioavailability. However, its nanoformulations are reported to have greater effects in cancer therapeutics by targeting tumors and reducing the dose required [31]. Quercitrin-PLA nanoparticles showed higher intestinal absorption, greater stability and better permeability to plasma membrane than quercitrin [32]. Similarly, Artemisinin, although having poor solubility, instability and an initial burst effect in its inherent form show better solubility and prolonged drug release as an anticancer drug after nanoencapsulation [33].

A number of nanomaterials such as nanoparticles, liposomes, micelles, polymerosomes, spheres etc. with promising application potential are being investigated for the diagnosis, imaging, and therapy of cancers [17-19,31,34]. Nanobased combination drug delivery, with enhanced therapeutic effects and fewer side effects is becoming an effective strategy for successful delivery of anticancer drugs [34].

Nanomedicine has an important role in ongoing changes in the antimicrobial field and several nanoformulations have already been marketed for bacterial diagnosis, antibiotic delivery, and medical devices [35].

Nanosized drugs can effectively reach their intended targets, reduce the cost and side effect and more acceptable and accessible to general public [12]. Such drug delivery systems are expected be highly commercialized and easily available in near future. Recent years have seen the advancement in the area of nanomedicine with the successful introduction of novel approaches like polymer and liposome based drug delivery systems, leading to more efficient therapeutic and diagnostic interventions [36]. This indicates brilliant future of novel herbal drug delivery systems, which are expected to enhance the therapeutic activity and overcome problems attributed to natural products and herbal medicine [11]. Nevertheless, potential toxicity and adverse effects of nanoformulations should give due consideration before their commercialization [12,25].

Conclusion

Efficacy of many traditional herbal drugs is limited due to their bulky size that limits their bioavailability and bioactivity. Novel drug delivery systems have tremendous potential in improving their bioavailability, pharmacokinetic profile, blood brain barrier and sustained delivery. This will enhance the efficacy of conventional drugs and provide several health benefits to the people. It is equally important to ensure the safety and simultaneous studies should be carried out on their potential toxicity.

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