

## RECENT DEVELOPMENT OF HERBAL FORMULATION- A NOVEL DRUG DELIVERY SYSTEM

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### ABSTRACT

The practice of drug delivery has changed dramatically in last few decades and even greater changes are welcome in near future. Due to recent development in technology various kinds of drug delivery devices has entered in routine health sector. Herbal drug sector is growing fast but somewhere due to its unconventional drug dosage it's not widely used by people. The drug of herbal origin can be utilize in better advanced formed with enhance efficacy by incorporating in modern dosage form. With the use of these advance techniques it gives us protection from toxicity, enhancement in stability, improved bioavailability of herbal formulations. Protection from physical and chemical degradation can be achieved. Prove beneficial to combat with life threatening disease more rapidly. Due to its patient friendly form it can be quickly adopted by people.

**Keywords:** Herbal formulation, Advantages, Disadvantages, Phytosomes, Ethanosomes, Novel drug delivery.

### INTRODUCTION

Ayurveda is ancient science of Indian system of medicine. Traditional formulation contain plant material as its core ingredient. In Ayurveda *Swarasa* (Juice), *Kalka* (Paste), *Kwath* (Decoction), *Sheeta kashyay*, *Phanta* are considered as drug delivery devices. All of them had very low shelf life hence the introductions of rolled pills, e.g. Gutika, Vatika, Fermented syrups e.g. *Asasva* and *Arishtas*, Medicated oil e.g. *Siddha tailas*, *Koopipakva rasayana* comes in place. As it exhibit better preservation quality and enhance therapeutic effect. But all of them has their own restriction. Where all constituent may or may not be come in formulation as some of them are water soluble or lipid soluble in nature.

Herbal drug itself is complex structure of many active constituents; As all of

them provide synergistic action and enhance the therapeutic value. Constituents like Flavanoides, Tannins, Terpenoides when incorporate into novel techniques show enhance bio available activity and targeted action at low therapeutic dose. Traditional herbal formulations show efficacy but drug delivery device has lack of scientific justification, standardization, and identification of single chemical constituent in complex poly herbal formulation.

#### Disadvantage of current drug delivery system used in Ayurveda. <sup>[1]</sup>

- Bulk dosing
- Decrease bioavailability and decrease absorption
- Show poor effect or require high amount of dose to produce desire effect.

- High amount of raw material require processing the medicine.
- Loss 'N' number of extinct or rare species.
- Harmful effect on ecology which ultimately become cause of global warming.
- No target specificity in present formulation.

**Advantage of novel drug delivery system.** <sup>[2]</sup>

- Help to increase the efficacy and reduce the side effect of various herbal compounds.
- Quantity of component becomes less with improving quality of drug effect.
- Fewer raw material are required to achieve the desire effect and control drug delivery to provide exact specification regarding drug dose form.
- Ready to use devices are acceptable in today's fast life style where time is important.
- Carry maximum amount of drug to the site of action by passing all barriers. Such as acidic pH of stomach increase prolong circulation of drug into blood due to their small particle size.
- Reduce repeat dose administration.

The main aim for adaptation of novel drug delivery devices in herbal formulations are to develop better system for proper drug delivery in terms of

- Target oriented
- Sustain and Controlled release of drug at the site which help to increase the efficacy and reduces side effects at the site of formulation.
- This administration not only reduces repeat administration but also helps to increase the therapeutic value by reducing toxicity and increase the bio-availability.

- Nowadays supercritical CO<sub>2</sub> extracts of herbs are use in many formulation as it contain most of active constituents hence new drug delivery system is perfect for such extract for better therapeutic effect.

**MATERIAL AND METHODS**

Various literary review has been studied to gain the information about novel drug delivery system and implication of herbal formulations. The aim of this article is to present an overall view of the current strategies to adapt for the formulation and application of herbal remedies, as well as help to conserve the environment by taking least amount of medicine to show its desire effect.

Traditional way of medication depends on supply of active compound. Most of the active compounds are highly soluble in water but less get absorb during circulation which in term less bio available to use. In modern technology effective chloroform alcohol extract are available which is not suitable for oral consumption. this present article is to summarize the different types of novel drug delivery device which can used in herbal formulation as they can improve drug efficiency, increase patient compliance, comfort and reduced total cost. Herbal drug technology has entered into a novel approach of developing various devices for herbal drug delivery. Thus, the present review focuses on novel drug delivering devices development.

**1. Phytosome**

This dose drug form is useful in case of water soluble phyto constituents( like tannins, terpenoids) which are poorly absorb either due to their large molecular size which is difficult to absorb in passive diffusion or which has poor lipid solubility result in poor bioavailability of drug. It is able to permeate the hydrophilic botanical extract to better absorption in intestinal

lumen. Phytosomes are prepared by complexing the polyphenolic phyto constituents in the ratio of 1:2 or 1:1 with phosphatidyl choline. The chemical bonds are formed in between phosphatidylcholine molecules, so it shows good stability.

A novel hesperetin was developed by combining and complexing hesperetin with hydrogenated phosphatidyl choline. Mukherjee *et al.* (2008) also studied its antioxidant activity and pharmacokinetic studies in CC14 intoxicated rats along. The results of the study showed the phytosome has shown high antioxidant activity. Pharmacokinetic studies have revealed the improved bioavailability of phytosome than the parent molecule at the same dosage.<sup>[3]</sup>

## 2. Liposomes

Liposomes are constructed with polar lipid which are made up of lipophilic and hydrophilic group of same molecule. Vesicle which are colloidal and spherical in shape entrapped an aqueous core which contains medicine in it to enhance product performance by enhancing its solubility, improving bio availability, targeting at the site of action and prolonged release of drug. Multiple herbal formulation now a day's are based on liposomal technology, but still it need improvement as major limitations of these techniques are like low encapsulation, efficiency, rapid leakage of water soluble drug in the presence of blood component and poor storage facility.

Liposomes with Green Tea and *Gaultheria procumbens* extract were prepared using lipid film hydration method and the optimum ratios of the component were determined. Herbal liposomes were characterized for their vesicle size, shape, encapsulation efficiency, drug content and in-vitro drug release study. Highest encapsulation efficiency (70.0%) and in-vitro drug release (95.2%) was achieved with

formulation. Liposomal formulations have been incorporated into carbopol gel base and found to be more superior against *Micrococcus luteus*.<sup>[4]</sup>

## 3. Emulsion

Emulsion are biphasic system in which one phase is immediately dispersed in other phase one phase is always water another phase is liquid/ oil. They have higher surface area hence they can penetrate through skin, non toxic and non irritant in nature. high solubility in skin hence high bio availability. The palatability of the non-emulsion compound and compatibility with other excipients are two major limited factors in this drug delivery device. The micro-emulsion is called as nanoemulsion and sub-micro emulsion is called as lipid emulsion.

The nanoemulsion formulation containing Neem oil (*Azadirachta indica*), Tween 20 and deionized water was successfully optimized by the high-energy method. A smallest droplet size of 31.03 nm was obtained. Neem oil nanoemulsion with the smallest droplet size was found to be more effective in controlling mosquito larvae compared with larger droplet sizes. Neem oil nanoemulsion may be a good alternative to other pesticides for the control of vector-borne diseases. Droplet size of 31.03 nm has been reported.<sup>[5]</sup>

The reduced size and uniform spreading of these fine particles increased the efficacy. The nano emulsion is easily affordable, economically feasible and moreover less toxic than synthetic pesticides, and may be used as an alternative for control of vector-borne disease.

## 4. Microsphere

It is also called as micro particle. microsphere consists of spherical particle diameter range from 1  $\mu\text{m}$  to 1000  $\mu\text{m}$ . each particle of drug is dispersed in particle. it is manufactured by various kind of

material. A series of plant active ingredient i.e. Rutin, Zedoras extract has been used to make micro particle. According to current reports on non biodegradable microsphere; polylactic acid is only polymer approved to be used by people. Solid and heavy microsphere is used for different application while hollow is used as additives to lower the density of material. They can be used for ingested or injected purpose. it can be used as site specific delivery of drug.

Curcumin (isolated from *Curcuma longa*) is the active ingredient of the Herb, turmeric, Curcumin floating microspheres were successfully developed using emulsion solvent diffusion method. The microspheres had good yield and showed high, drug entrapment efficiency. The flow properties of microspheres were within the acceptable range and therefore would be easily filled into capsules. Release properties were satisfactory and the formulations hold promise for further development into drug delivery systems for oral administration of curcumin. And development and Evaluation of Floating Microspheres of Curcumin. [6]

### **5. Ethosomes**

Ethosomes are developed by mixture of phospholipids and high concentration of ethanol. This carrier can penetrate through the skin deeply lead to improve drug delivery into deeper layer of skin and in blood circulation. These formulation are useful for topical delivery of alkaloids in form of gel and cream for patients comfort. They show increase in their permeability through the skin by fluidizing the lipid domain of the skin. Unstable nature and poor skin penetration are limits for Ethosomes tropical delivery.

The Ethosomes was developed and examined for their ability the topical absorption of Tetrandrine through dermal delivery, and the relation of formulations to

the pharmacological activity of Tetrandrine loaded in the formulation was also accessed. Result of the drug levels in rat plasma showed that when Tetrandrine-loaded Ethosomes were topically administered in rats the drug level was low to be detected in rat plasma. By providing fewer delivery of Tetrandrine into bloodstream, topical administration might offer favorable efficacy with reduced side effects, thus leading to improve patient's compliances. In conclusion, Ethosomes were demonstrated to be promising carrier for improving topical delivery of Tetrandrine via skin. [7]

### **6. Tran dermal drug delivery**

Tran dermal drug delivery is carry out by a patch that is attached to the body surface. This patch is a medicated adhesive pad that is design to release the active ingredient at a constant rate over a constant period of several hours to days after application to the skin. The drug present in transdermal patch permeates into systemic circulation by diffusion through various layer of skin which lead further to effected organ. This system provides drug delivery at control rate, high bio availability, easy application, sustainable action. Limitations are hepatic first pass metabolism, maintenance of steady plasma level of drug.

*Momordica charantia* is traditionally used as a medicine for Diabetes. The Transdermal film contain the fractionated component from Ethanolic extract of *M. chirantia* fruits were prepared by using hydroxy propyl methyl cellulose as a polymer. The films were evaluated for folding endurance, thickness, weight variation, drug contents and in vitro diffusion studies and in vivo parameters like acute and sub-acute anti hyperglycemic activity in diabetic rats, the percentage release of active constituents from Trans dermal patches of *M. charantia* (2cm<sup>2</sup>; 10 mg/patch) was

found to be satisfactory. The Transdermal route exhibited negligible skin irritation and in vivo results revealed that the patches successfully decrease the blood glucose level and have been found to be effective for diabetes through modern pharmaceutical formulation techniques.<sup>[8]</sup>

### 7. Micro pellets

Micro pellets is an agglomeration process that converts fine powder or granules of bulk drugs and excipients into small, free flowing semi spherical units. Pellets being multi particulate. systems are widely used due to the technical as well as therapeutic advantages over single unit dosage form. e.g. Inoherbs micropellets contain active herbal compound( Phyto-granules).

The extract of *Andrographis penniculata* was entrapped into micro pellets of calcium alginate. So formed pellets were evaluated for hepatoprotective activity in paracetamol induce hepatotoxicity in rat. The bitter alginate micro pellets loaded with alcoholic extract of *A. penniculata* were successfully inhibit the paracetamol induce hepatotoxicity by decreasing ASL, ALT, and liver weight.<sup>[9]</sup>

### 8. Nano particle

In this system mean particle size of medicine is small up to 100nm. Due to reduction in size it gives increase compound solubility, reduce medicinal dosage and improve the absorption rate of herbal drug. e.g. nanonized curcuminoides. Zedory turmeric oil, a traditional Chinese medication was loaded with nano structured lipid carriers after doing several in vitro drug test it indicate that prepared nanoparticle enhance the drug release rate which shows promising IV dosage form of water insoluble oily drug. These nano carriers have been made up of safe synthetic biodegradable polymer material. in this formulation

both lipophilic and hydrophilic drugs can be loaded.

fucose- chitosan/ heparin nanoparticle-encapsulated berberine was prepared and delivery efficiency was monitored by confocal laser scanning microscopy. Analysis of stimulated gastrointestinal medium indicated that the proposed drug carrier effectively controls the release of berberine, which interacts specially at the site of *H.pylori* infection, and significantly increases berberine's suppressive effect on *H.pylori* growth. In an *in-vivo* study, the berberine-loaded fucose-conjugated nanoparticles exhibited an *H.pylori* clearance effect and effectively reduce gastric inflammation in an *H.pylori* infected animal study.<sup>[10]</sup>

### 9. Polymeric Micelle formulation

These are formed from amphiphilic blocks have been successfully used for delivery of drug that lack of water solubility. the characteristic feature of micelles such as particle size, shape, drug loading, cellular internalization, stability and release kinetics of drug can be improved by altering the physicochemical properties of the constituents block copolymers and method of preparation.

Thermo sensitive co-polymeric micelle synthesized by radical copolymerization and extract of *Nigella sativa* is entrapped in this polymeric system to evaluate its antibacterial activity. *Nigella sativa* loaded polymeric micelle found more effective than other form. the thermo sensitive polymeric system would more effectively release the drug into body when infectious status are functional.<sup>[11]</sup>

## DISCUSSION

Various technologies has been introduced in last few decades. We accept Ayurvedic kalapa in their original form. they either made in water soluble form like *Kalka* or *Swaras* or in oil form like *Ghrita*

or *Taila*. where all constituent may or may not be come in formulation but when we use active constituent of certain herbal drug in new drug technology we can make sure that all active constituents are come in drug delivering device like Phytosomes, Ethosomes, Transderm etc. They are among new dose form which we can implement instead of Tablets, Pills. which not only reduce the drug dose but also prove to beneficial in terms of high efficacy, high bioavailability, low dose, low making cost and eco friendly help to conserve nature. New dosage form are good for in terms of longevity and beneficial to prove the efficacy.

### CONCLUSION

There is great potential lied in development of novel drug delivery system for herbal formulation as its safe, effective, convenient and economically affordable drug delivery. it can lead to overcome the problem associated with herbal formulation. results in enhance its efficiency and make is more bio available by increase its solubility, controlled release and target oriented.

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**Table: Application of Few Herbal Novel Drug Delivery System**

Herbal Formulation	Application	Pharmacological Activity	Routes of Administration	Ref
Quercetin phytosomes	Exerted better therapeutic efficacy	Anti oxidant, Anti-cancer.	oral	12
Colchicin liposomes	Enhance skin accumulation	Antigout	Topical	13
Azadirachta indica emulsion	The formulation has sustain release	Anti-fungal, Antibacterial	Topical	14
Rutin Microsphere	Targeting into Cardiovascular region.	Cardiovascular drug	Oral	15
Matrine ehtosome	Increase cutaneous permeation	Anti tumor, Anti inflammatory	Topical	16

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