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Review Article

Development of Suitable Pharmaceutical Dosage forms through Herbal Plant Extract

Gadapa Sri Divya*, K. Geetha, A. Pratyusha, V. Uma Maheshwar Rao

CMR college of Pharmacy, Kandlakoya (V), Medchal Road, Hyderabad-501401, Telangana, India

***Corresponding Author: Gadapa Sri Divya**

Email Id: sri.gadapa@gmail.com

ABSTRACT

In recent years there is a spurt in the interest regarding survival of Ayurvedic forms of medication. In the global perspective, there is a shift towards the use of medicine of herbal origin, as the dangers and the shortcoming of modern medicine have started getting more apparent, majority of Ayurvedic formulation are prepared from herbs. It is the cardinal responsibility of the regulatory authorities to ensure that the consumers get the medication, which guaranteed the purity, safety, potency and efficacy. As a result of this Standardization arise for maintaining a good coordination among the quality of raw herb material, in process materials and in final product. Present study was carried out to standardize different types of formulations using pharmaceutical excipients.

Key words: Herbal medicine, Excipients, herbal extracts, Tablets, Gels.

INTRODUCTION

In the few decades, there has been exponentially growth in the field of herbal medicines. Nature always stands as a golden mark to exemplify the outstanding phenomena of symbiosis. Today about 80% of people in developing countries still relay on traditional medicine based largely on the different species of plants for their primary health care. About 500 of plants with medicinal uses are mentioned in ancient literature and 800 plants have been used in indigenous system of medicine. The various indigenous systems such as Ayurveda, siddha, unani use several plant species to treat different ailments Tyler defines herbal medicines as "crude drugs of vegetable origin utilized for the treatment of disease states, often of a chronic nature, or to attain or maintain a condition of improved health. "Current demands for herbal medicines have resulted in an annual market of$1.5 billion and increasingly widespread availability.[2] Many dosage forms formulated today are complex system containing many other components along with the active pharmaceutical ingredient (API); these compounds are generally added along with the active pharmaceutical ingredients in order to protect, support or enhance stability of the formulation. Most of the times it is observed that the active pharmaceutical ingredient in its pure form does not retain its stability for long which results in its denaturation, or sticking to the container wall thus

rendering it unfit, hence in order to stabilize the API excipients are added which aid in maintaining the stability of the product and ensures that API retains its stability for a considerable period of time thus improving the shelf life of dosage formulation.

- Bulk up the formulation in case of potent drug for assisting in formulation of an accurate dosage form.
- Improve patient acceptance.

HELP IMPROVE BIOAVAILABILITY OF ACTIVE DRUG[3]

Excipients usually help in improving the bioavailability of the active pharmaceutical ingredient for e.g. In many cases an active substance (such as aspirin) is not absorbed easily by human body in such cases the active ingredient is dissolved in or mixed with an excipient which may either act as solvent or assist in absorption of the drug in human body. Enhance overall safety and effectiveness of the formulation during its storage and use.

These components are generally termed as excipients and according to the international pharmaceutical excipient council, Excipient is defined as "Any substance other than active drug or pro-drug that is included in the manufacturing process or is contained in finished pharmaceutical dosage forms". The US pharmacopoeia-National formulary (USPNF) categorizes excipients according to the functions they perform in the formulations e.g. Binders, disintegrants etc. Excipients can be classified on the basis of their origin, use in dosage form, and functions they perform as follows

EXCIPIENT BASED ON THEIR ORIGIN[4]

Animal source: - Lactose, Gelatin, Stearic acid, Bees wax, Honey, Musk, Lanolin etc.

Vegetable source: - Starch, Peppermint, Turmeric, Guar gum, Arginates, Acacia etc.

Mineral source: - Calcium phosphate, Silica, Talc, Calamine, Asbestos, Kaolin, Paraffin, etc.

Synthetic: - Boric acid, Saccharin, Lactic acid, Polyethylene glycols, Polysorbates, Povidone etc.

The following tables gives a classification of various excipients used in pharmaceutical dosage forms: (*table no 1,2,3)*

CLASSIFICATION OF EXCIPIENTS BASED ON THEIR FUNCTIONS 10-13

Excipients are classified on the basis of the functions they perform such as:-

Various excipients used in solid dosage forms perform various functions like:-

Binders, diluents, lubricants, disintegrating agent's plasticizers etc, e.g.: when 5% starch is used in formulation it acts as a binder for tablet formulations where as when it is used in dry form it can perform the function of a disintegrant.

EXCIPIENTS THAT ARE USED IN LIQUID DOSAGE FORMS ARE

Solvents co- solvents, buffers anti-microbial agents emulsifying agents sweetening agents, flavors, etc

SOME EXCIPIENTS HAVE THERAPEUTIC VALUES WHICH ARE CLASSIFIED AS UNDER

Anesthetics 10:- chloroform, etc

Laxatives: - bentonite, psyllium, xanthan gum11, guar- gum etc.

Ph modifiers: - citric acid.

Astringent: - cinnamon, alum, zinc sulphate.

Carminative: - cinnamon13, dill water, anise water.

Nutrient sources: - agar12, lactose, etc.

Table no 1: Excipients used in solid dosage forms[6,7]

Excipient category	Function in formulation	Working principle	Examples
Diluents	Fillers	Make up the bulk of solid unit dosage forms when drug itself is inadequate to produce the bulk.	Lactose, Directly compressible Starches, Dextrose, Sorbitol, Microcrystalline cellulose, Dibasic Calcium phosphate dehydrate.

Binders and Adhesives	Impart cohesive qualities to powdered material.	Improves free flow qualities by formulation of granules to desired hardness and size.	Acacia, Gelatin, Starch paste, Polyvinyl pyrrolidone, Glucose, Carboxymethyl cellulose, Povidone.
Lubricants	Reduce inter-particular friction, prevent adhesion of tablet material to the surface of dies and punches facilitate easy ejection of tablet from die cavity and improve the rate of flow tablet granulation	Interpose a film of low shear strength that interface between the tabletting mass and die wall	Talc, Stearic acid, Magnesium stearate, Calcium stearate, Polyethylene glycol, Surfactants, vegetable oil.
Glidants	Improve flow characteristics of powder mixture.	Added in dry state prior compression, it reduces friction between particles.	Colloidal Silicone dioxide (Carbosil), Asbestos free starch, Corn starch.
Disintegrants	Facilitate breakup or disintegration after administration	Function by drawing water into the tablet, swelling it and causing the tablet to burst apart.	Starches, Clays, Cellulose, Cross linked polymers, Modified starches such as Primogel and Explotab, Veegum HV.
Superdisintegrants	Improved disintegrant efficacy resulting in decreased use levels when compared to traditional disintegrants		Crosscarmalose, Cross Povidone, Sodium starch glycolate.
Coloring agents (these must be approved and certified by F.D.A)	Impart aesthetic appearance to dosage form, disguising off color drugs, product identification.		FD and C, D and C dyes and lakes.
Flavors	Limited to chewable tablets/ tablets intended to dissolve in mouth.	Mask unpleasant taste	Spray dried and other flavors, syrups etc.
Sweeteners	Impart sweet taste to the formulation; use is limited to chewable tablets.		Mannitol, Saccharin.etc
Sorbents	Moisture proofing	Limits the fluid sorbing, taking up of liquid or gas either by adsorption or absorption in dry state.	Silica gel, activated carbon, clay Etc

Coating materials	Protect tablet ingredients from detoriation by moisture, help swallowing unpleasant tasting tablets		Hydroxypropylmethyl cellulose (HPMC), Synthetic polymers, Shellac, Corn protein Zein, Polysaccharides, Capslues coated by Gelatin, Povidone, Ethyl cellulose.
Plasticizers	For soft gelatin capsule preparation, gelatin based suppositories, film coated tablets etc.	Produce elasticity and flexibility to the coating materials in case of tablets, determine hardness of capsule shell in case of soft gelatin capsule and impart softness and resilience to suppositories.	

Table no 2: Excipients used in liquid dosage forms [8]

Excipient category	**Function in formulation**	**Working principle**	**Examples**
Solvents	Dissolving solute/Active pharmaceutical ingredient.	Breaking of bonds and reducing effective charge on ions thus increasing Solute-Solvent forces of attraction which are eventually greater than Solute-Solute and Solvent-Solvent forces of attraction.	Water, alcohol, acetic acid, acetone, ethyl acetates, syrups, etc.
Co solvents	Increase the solubility of solute in solvents.	Co-solvent system works by reducing the interfacial tension between predominantly aqueous solutions and hydrophobic solutes.	Ethanol, Sorbitol, Glycerin, Propylene glycol etc.
Buffers	Maintain pH of the formulation.	Act by binding hydrogen ions in acids and donating hydrogen ions in bases	Phosphate buffers, Acetate buffers, Citric acid Phosphate buffers etc
Antimicrobial preservatives.	Prevent microbial growth in formulations.	Bacteriostatic action	Benzyl alcohol, Butyl paraben, Phenol, Thiomersal etc.
Antioxidants	Control oxidation.	Act by getting preferentially oxidized or by blocking an oxidative chain reaction.	Ascorbic acid, Sodium bisulphate, Thiourea, Butyl Hydroxy Toluene (BHT), Tocopherols.etc

Wetting agents	Aid wetting and dispersion of hydrophobic active pharmaceutical ingredients.	Act by reducing interfacial tension between solids and liquids in suspensions.	Sodium Lauryl Sulphate (SLS), Tween 80, Spans, Lecithins etc.
Antifoaming agents	Discourage formation of stable foam.	Lowers surface tension and cohesive binding of liquid phase.	Simethicone, Organic phosphates, Alcohols, Paraffin oils, Sterates and glycols.
Thickening agents.	Prevent settling/sedimentation, Modify viscosity.	Work by entrapment of solid particles.	Methyl cellulose, Hydroxyethyl cellulose, Microcrystallince cellulose etc.
Humectants	Retard evaporation of aqueous vehicles from dosage forms	They are hygroscopic in nature which helps in preventing evaporation of solvent.	Propylene glycols, Glycerol, Polyethylene glycol etc.
Chelating agents.	Protect drug from catalysts that accelerate the oxidative reaction	Chelating agents form complexes with metal ions inactivating their catalytic activity in oxidation of medicaments	Disodium EDTA, Dihydroxy ethyl glycine, Citric acid and Tartaric acid.
Emulsifying agents	Prevent coalescence of the dispersed globules.	Forms barriers at interface, and reduces interfacial tension.	Sodium Lauryl Sulphate, Cetrimide, Macrogol esters, Sorbitan esters etc.
Flocculating agents.	Prevent caking	Addition of an electrolyte reduces the magnitude of zeta potential of dispersed particles.	Starch, Sodium alginate, Carbomer.etc.
Sweetening agents	Impart sweetness		Sucrose, Sorbitol, Saccharin, Aspartame, Sucralase
Colors.	Impart flavor		Amaranth, Erythrosin, Eosin, Tartarazine etc.
Flavors	Impart flavor		Aromatic waters, Syrup etc
Excipient used in aerosol Propellant	Developing pressure in container which expels the product		Trichloromonofluoromethane, Dichlorodifluoromethane, Etc.

Table no 3: Excipients used in semisolid dosage forms[9]

Excipient category	**Function in formulation**	**Examples**
Structure forming excipients	Form gel like structure	Cetosterly alcohol, sorbiton and other hydrophilic surfactants , fluid hydrocarbons like mineral oils etc
Preservatives	For preserving the formulation	Benzyl alcohol, proply paraben, methyl paraben,

		chlorocresol, imidazolidinyl urea, sodium benzoate etc
Antioxidants	Prevent oxidation	Butyl hydroxy toulne , butyl hydroxy anisole, ascorbic acid etc
Solubilizers	Enhance solubility of the active ingredient in ointments	Lanolin, cholesterol or cholesterol esters
Gelling agents	Form gels	Carbomer934, pemulen®, carboxy methyl cellulose, hydroxy propyl cellulose, xanthan gum etc
Emollients	Modify vehicle/skin characteristics to assist penetration of active ingredient through skin	Glycerin, mineral oil, petrolatum, isopropyl palmitate etc
suppository bases	Used to form base for dissolving active ingredient	Cocoa butter, glycerin, coconut oil, gelatin, hydrogenated vegetable oil, polyethylene glycol etc

EXCIPIENT SELECTION[14]

Excipients can be considered as indispensible component of medicinal products and in most of the formulations they are present in greater proportion with regards to active pharmaceutical ingredient, as it forms the bulk of the formulation it is always necessary to select an excipient which satisfies the ideal properties for a particular excipient. Excipient selection generally focuses on the desirable characteristics of excipients such as functionality, material consistency, regulatory acceptance, cost, availability, and sources. Material properties like micromeritics, chemical thermal rheological, mechanical etc also play an important role in development of drug formulation. Formulators must also consider physicochemical properties, stability and compatibility issue, pharmacokinetic attributes, permeation characteristics, segmental absorption behavior, drug delivery platform, intellectual property issues etc while selecting an excipient for formulation development, this may help in determining the absorption challenges and desired delivery platform for active pharmaceutical ingredients. The concept of quality by design (QbD) helps in understanding excipients normal variability and its potential impact on the processes of formulation development can be achieved. Excipient compatibility tests allows us to determine drug excipient interactions which can be either avoided or can be modified to utilize in an efficient manner which helps in minimizing the risk associated with the excipients. Excipient selection also depends on various routes of administrations. Excipient selection must be done on the basis of characteristics an excipient offers. The ideal characteristics of an excipient are given as under:-

An excipient must be:-

- Chemically stable
- Non-reactive
- Low equipment and process sensitive
- Inert to human body
- Non toxic
- Acceptable with regards to organoleptic characteristics
- Economical
- Having efficiency in regards with the intended use.
- Excipients even though considered inert substance, have the tendency to react with drug components, other excipients, and also the packaging system. Excipients may also contain various impurities which may result in decomposition of the active pharmaceutical ingredients in the formulation thus altering the shelf life of the formulation.

Plants have long served mankind as source of medicinal agent. Natural products have once served as source of all drugs. Herbal medicine involves the use of leaves, stem, flowers, fruits, seeds, roots rhizome and bark for healing of diseases. There can be little doubt that, the use of plants for healing purpose is the most ancient form of medicine known. The quest of the plant with medicinal properties

continues to receive attention as scientists are in need of plants particularly of ethno botanical significance for a complete range of biological activities, which ranges from antibiotic to anticancerus. Several plants and herbs species used traditionally have potential antimicrobial and antiviral properties and this has raised the optimism of scientists about the future of phyto antimicrobial agent. For most herbs, the specific ingredients that cause a therapeutic effect is not known, whole herbs contain many ingredients and they likely work together to produce the desired medicinal effect. These components work together to produce therapeutic effects, lessen the incidence of side effects and enhance effectiveness, synergistic action and reduce toxicity. Most herbal medicines are well tolerated by the patient with fewer unintended consequences than pharmaceutical drugs. Herbs typically have fewer side effects and may be safer to use over a long period of time. Herbal medicines tend to be more effective for long standing health complaints that do not respond well to conventional medicines, they have lower costs and are readily available and accessible compared to conventional medicines. Formulation studies involve developing a preparation of the drug which is both stable and acceptable to the patient. Herbal formulation means a dosage form consisting of one or more herbs or processed herbs in specified quantities to provide specific nutritional, cosmetic and/or other benefits meant for use to diagnose, treat, mitigate diseases of human beings or animals and/or alter the structure or physiology of human beings or animals[16].

DOSAGE FORM

Dosage form is a mixture of active drug components and non drug components or excipients. There are several forms of dosage forms, which can generally be classified as solid dosage form, liquid dosage form and semisolid dosage form. Drugs are usually not administered as pure chemical substances alone but are almost always given as formulated preparations. These can vary from relatively simple solutions to complex drug delivery systems through the use of appropriate additives or excipients in the formulation (Aulton, 2007). Excipients provide various pharmaceutical functions, these include solubilisation, suspending, thickening, emulsifying, modifying dissolution, improving the compactibility and flavoring drug substances to form various medicines or dosage forms. Formulation development is the development of bioactive stable and optimal dosage form for a specific administration route. This involves the use of excipients which ensures that the therapeutic performance, the safety parameters and the stability of the active drug substance is not compromised (Oradifiya, 2009).

HERBAL MEDICINES FORMULATION

A herbal medicine formulation is any medicinal product exclusively containing one or more herbs or processed herb in specified quantities as the active ingredients to provide specific therapeutic, nutritional, cosmetic and other benefits. These formulations are obtained by subjecting herbal substances to various treatments such as drying, extraction, distillation, expression, fractionation, purification, concentration, fermentation etc., standardizing and then incorporating the appropriate excipients. Extraction of active ingredients from plants began in the early 19th century when chemical analysis became available, later chemists began making their own version of plant compounds and over the time, the use of herbal medicines declined in favour of synthetic drugs. However, recent interest in herbal medicines due to increased and advanced research, safety, availability and lower cost has led to the need to produce more formulations to meet demand. Herbal formulations come in different forms, these include decoctions, capsules, tablets, creams, gels, ointments, tinctures, suppositories and even some novel forms such as extended release, sustained release and microencapsulating dosage forms (Musthaba *et al*., 2010). The most common dosage forms of herbal preparations are liquids derived from macerations, infusions and decoctions, with the associated problems of large dose volumes, difficult packaging and poor stability. Solid preparations such as capsules and tablets on the other hand often have higher stability and are easier to standardize which adds to an increase in their therapeutic acceptance, efficacy and product value. Large scale production of herbal medicines which is as a result of commercialization of herbal medicines requires that scientists and manufacturers maintain the quality and safety of these herbs, as such assurance of quality, safety and efficacy medicinal plants and herbal products have become very important.

HERBAL EXTRACT

Extracts are defined as a concentrated preparation of a liquid, powder or viscous substance ordinarily prepared from dried plant using an appropriate solvent. These are obtained by removing the active constituents from a part of raw herbs often using suitable solvents such as alcohol and water, evaporating all or nearly all the solvent and adjusting the residual mass to a prescribed standard. They may be obtained in powder form, aqueous form or the tincture form. Most liquid dosage forms are produced from fluid extracts whiles most solid dosage forms are produced from solid extracts. It is these extracts that usually serve as the active ingredients in the formulation of herbal preparations.

DECOCTIONS

Decoction is a method of extraction by boiling to dissolve chemicals, from herbal or plant material, which may include stems, roots, bark and rhizomes. Decoction involves first mashing, and then boiling in water to extract oils, volatile organic compounds, and other chemical substances. Decoction can be used to make teas, coffees, tinctures and similar solutions. It is used for seeds, roots and bark and other parts of the plant that will not release their medicine at lower heat levels. This method of extraction is used in plants whose medicinal properties are not harmed by the application of heat. Decoctions are easy to prepare, however, they are not easy to keep from microbial contamination, long term storage is problematic as active principles may be quite unstable, also traditional measurements and directions are not exact. Generally, decoctions are inconvenient and unpleasant herbal preparations to take.

CAPSULES

Capsules are solid dosage forms in which the drug is enclosed within either a hard or soft soluble container or shell. The hard-shelled capsules are normally used for dry, powdered ingredients or miniature pellets whiles soft shelled capsules are primarily used for oils and for active ingredients that are dissolved or suspended in oil. Capsule shell is an excellent barrier to air, easy to swallow and tasteless, may allow rapid release and flexibility of formulation. Capsule shells are usually formed from gelatin, they may however be formed from starch or other suitable substances (USP, 2007). The hard shell capsule sizes range from No.5 which is the smallest to size 000 which is the largest, except for veterinary sizes. (USP, 2007). Often capsule of herbs are concentrated for more strength and they are easily portable. Excipients commonly used in capsule formulation are diluents, glidants, disintergrants, lubricants and wetting agents. Hard gelatin capsules usually require between one and four excipients. However there are some drugs in capsule form that contains only the active ingredient, which means there is no excipient. Most of the strongest medicinal herbs are quite bitter to taste, so it is easier to get them down when taking them in capsule form. A capsule should be able to disintegrate in the stomach followed by the dissolution of the contents in the fluids of the gastrointestinal tract; as such disintegration tests and dissolution tests are conducted on capsules.

TABLETS

A tablet is a pharmaceutical dosage form which comprises a mixture of active substances and excipients usually in powder form, pressed or compacted into a solid dose. Tablets are the most popular dosage form in use today because they are simple and convenient to use. They are cost effective, convenient to dispense in stores and easy for patient to administer, an accurately measured dosage of the active ingredient in a convenient portable package, and can because it is a dry dosage form, it is stable and has a long shelf life. However, preparation of tablets requires the use of excipients such as diluents, binders and lubricants to facilitate the manufacturing process and also ensure that resulting tablets have the desired properties. Tablets should be sufficiently strong to withstand handling during manufacture and usage, they should also disintegrate and release the drug in a predictable and reproducible manner.

GELS

Gels are homogenous semisolid preparations usually consisting of solution or dispersion of one or more active ingredients in suitable hydrophilic or hydrophobic bases. They are prepared with the use of suitable gelling agent and are intended to be applied to the skin or certain mucous membranes for protection and/or therapeutic or prophylactic purposes. Gels may contain suitable auxiliary substances such as antimicrobial preservatives,

antioxidants and stabilizers (BP,1988). The interactions between the liquid vehicle and the colloidal particles are either physical or covalent, the vehicle is continuous and interacts with the colloidal particles within three dimensional network that is formed between adjacent particles. The vehicle may be aqueous, hydro alcoholic, alcohol based or non aqueous. The colloidal particles may be dispersed solids or dispersed polymers (USP, 2007).

OINTMENTS

Ointments are greasy, semi-solid preparations, often anhydrous and containing dissolved or dispersed medicaments intended for external application to the skin or mucous membranes. Herbal Ointments are used for topical applications and they are made by mixing powdered drugs are to be incorporated for local application should depend on the condition of the patient's skin, the biological effect desired, and the pharmaceutical compatibility of the ingredients with each other and the base. Ointment bases are classified into four major groups, these are hydrocarbon bases, absorption bases, water removable or emulsion bases and water soluble bases.

CREAMS

Creams are semi-solid dosage forms containing one or more drug substances dispersed in a suitable base that is mixtures of oil and water. They are divided into two types: oil-in-water creams which are composed of small droplets of oil dispersed in a continuous water phase, and water-in-oil creams which are composed of small droplets of water dispersed in a continuous oily phase. A cream is a topical preparation usually for application to the skin and also application to mucous membranes such as those of the rectum or vagina.

TINCTURES

A tincture is typically an alcoholic/water extract of plant or animal material or solution of such or of a low volatility substance such as iodine and mercurochrome. It is used when plants have active chemicals that are not soluble in water and/or when larger quantities is prepared for convenience and wanted for longer term storage. To qualify as an alcoholic tincture, the extract should have an ethanol percentage of at least 40–60%. In herbal medicine, alcoholic tinctures are made with various concentrations of ethanol with 25% being the most common. Other concentrations include 45% and 90%. Herbal tinctures are not always made using ethanol as the solvent, though this is most commonly the case. Other solvents include vinegar, glycerol, ether and propylene glycol, not all of which can be used for internal consumption. Ethanol has the advantage of being an excellent solvent for both acidic and basic constituents.

SUPPOSITORIES

A suppository is a drug delivery system that is inserted into the rectum (rectal suppository), vagina (vaginal suppository or pessary) or urethra (urethral suppository), where it dissolves or melts. They are used to deliver both systemically-acting and locally-acting medications. The principle is that the suppository is inserted as a solid, and will dissolve or melt inside the body to deliver the medicine pseudo received by the many blood vessels that follow the larger intestine. Alternative dosage forms for the rectal and/or vaginal route are tablets, capsules, ointments and enemas. Generally suppositories consist of a vehicle in which the drug is incorporated and in some cases additives are coformulated. A pharmaceutical pessary is used as a very effective means of delivery of pharmaceutical substances easily absorbed through the skin of the vagina or rectum, or intended to have action in the locality, for example against inflammation or infection, or on the uterus. There are two main classes of vehicles or suppository bases, the fatty base and the water soluble or water miscible bases.

CONCLUSION

Oral herbal dosage forms from herbal extract shows good elegance & palatability. Liquid dosage forms like Liquid Oral & Suspension having good stability on storage. Thus it can be concluded that these oral herbal dosage forms could be suitable dosage forms for *Herbal plant* extracts for commercial purpose.

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