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Natural Polymers-Promising Potential In Drug Delivery

Jyoti Sharma, Loveleen Kaur*, Neha Kanuja, Manju Nagpal, Rajni Bala

College of Pharmacy, Chitkara University, Chandigarh-Patiala National Highway, Rajpura– 140401, Patiala, Punjab, India.

***Corres. author: loveleenenator@gmail.com**

Abstract: Introduction: Polymers have been used as a main tool to control the drug release rate from the formulations. Extensive applications of polymers in drug delivery have been realized because polymers offer unique properties which so far have not been attained by any other materials. The family of natural polymers has great appeal to drug delivery as it comprises polymers with a large number of derivatizable groups, a wide range of molecular weights, varying chemical compositions, low toxicity, and biodegradability yet high stability.Various natural gums and mucilages have been examined as polymers for control and sustained drug release, in the last few decades. Natural polymers remain attractive primarily because they are commercial, readily available, capable of multitude of chemical modifications and potentially degradable and compatible due to their origin. Natural gums are among the most popular hydrophilic polymers because of their cost-effectiveness and regulatory acceptance. A number of plants extracts such as Moringa oleifera, Cyamopsiste tragonolobuos, Ocimum basilicum, Bursera bipinnata, Shorea wiesneri, Tamarindus indica etc have been widely used as excipients in various dosage forms for their binder and disintegrant action. These plant extracts also exhibit therapeutic effects such as hypolipidaemic action of Moringa oleifera, antimicrobial, antioxidant action of Ocimum basilicum etc thereby providing a synergistic action.
Future Potential: In coming decades, it is anticipated that natural polymers will be coming as additional derivatives for development of various novel drug delivery systems due to a number of actions such as coating agent, gel former, controlled-release matrix, in addition to inducing desirable properties such as mucoadhesion and permeation enhancement to improve oral bioavailability of a drug.
Keywords*:* Synergistic, Hypolipidaemic, Mucoadhesion, Cyamopsiste tragonolobuos, Shorea wiesneri.

INTRODUCTION

Recent decades have seen tremendous strides in the signing of novel dosage forms. But tablets still remain an attractive option for pharmaceutical scientists and clinicians because they offer advantages of accurate unit dosing, better patient compliance, ease of large-scale manufacturing, and low production cost (1). Regular research is going on for the use of natural occurring biocompatible polymeric material in designing of dosage form for oral controlled release administration (2). Biodegradable polymers have been widely used in biomedical applications because of their known biocompatibility and biodegradability. Biodegradable polymers could be classified into synthetic and natural (biologically derived) polymers. Both synthetic and natural biodegradable polymers have been used for drug delivery, and some of them have been successfully developed for clinical applications. This entry focused on various biodegradable polymers that have been used in development of drug delivery systems. Advances in organic chemistry and nano/micro fabrication/manufacturing methods enable continuous progresses in better utilization of a wide range of novel biodegradable polymers in drug delivery (3). Natural gums are among the most popular hydrophilic polymers because of their cost-effectiveness and regulatory acceptance (4). Natural gums are biodegradable and nontoxic,

which hydrate and swell on contact with aqueous media, so these have been used for the preparation of dosage form (2). Plant polysaccharides; have been shown to be useful for the construction of drug delivery systems for specific drug delivery (5). According to the original definition which meant broadly" plant exudates "the term encompassed also various resins, rubber latex, etc. The present definition of gums is somewhat narrower and more specific. It comprises all materials that can be dissolved or dispersed in water to form more or less viscous colloidal solutions or dispersion. Gums have been used as food and also for medicinal purposes by many civilizations. This article emphasizes a detailed description of various natural polymers along with potential applications.

Moringa oleifera

There are about thirteen species of Moringa trees in the family Moringaceae. *Moringa oleifera* Lam. (synonym: *Moringa pterygosperma* Gaertn.) is the most widely known species but other species deserve further research as to their uses (6).

Moringa oleifera is the most widely cultivated species of a monogeneric family, the Moringaceae that is native to the Sub-Himalayan tracks of India, Pakistan, Bangladesh and Afghanistan. This rapidly-growing tree (also known as the horseradish tree, drumstick tree, benzolive tree, kelor, marango, mlonge, moonga, mulangay, nébéday, saijhan, sajna or Ben oil tree), was utilized by the ancient Romans, Greeks and Egyptians; it is now widely cultivated and has become naturalized in many locations in the tropics. It is a perennial softwood tree with timber of low quality, but which for centuries has been advocated for traditional medicinal and industrial uses. It is already an important crop in India, Ethiopia, the Philippines and the Sudan, and is being grown in West, East and South Africa, Tropical Asia, Latin America, the Caribbean, Florida and the Pacific Islands. All parts of the *Moringa* tree are edible and have long been consumed by humans. *Moringa* seed oil (yield 30-40% by weight), also known as Ben oil, is sweet non-sticking, non-drying oil that resists rancidity. It has been used in salads, for fine machine lubrication, and in the manufacture of perfume and hair care products (7). In the West, one of the best known uses for *Moringa* is the use of powdered seeds to flocculate contaminants and purify drinking water (8, 9, 10). The seeds are also eaten green, roasted, powdered and steeped for tea or used in curries. This tree has in recent times been advocated as an outstanding indigenous source of highly digestible protein, Ca, Fe, Vitamin C, and carotenoids suitable for utilization in many of the so-called “developing” regions of the world where under nourishment is a major concern (11).

Nutritional Importance

Moringa trees have been used to combat malnutrition, especially among infants and nursing mothers. Three non-governmental organizations in particular-trees for Life, Church World Service and Educational Concerns for Hunger Organization-have advocated *Moringa* as “natural nutrition for the tropics.” Leaves can be eaten fresh, cooked, or stored as dried powder for many months without refrigeration, and reportedly without loss of nutritional value. *Moringa* is especially promising as a food source in the tropics because the tree is in full leaf at the end of the dry season when other foods are typically scarce.

A large number of reports on the nutritional qualities of *Moringa* now exist in both the scientific and the popular literature. *Moringa* leaves contain more Vitamin A than carrots, more calcium than milk, more iron than spinach, more Vitamin C than oranges, and more potassium than bananas,” and that the protein quality of *Moringa* leaves rivals that of milk and eggs (12, 13).

Pharmacological Importance:

Analgesic activity: The experimental studies using hot plate and tail immersion method have shown that alcoholic extract of leaves and seeds of *Moringa oleifera* possess marked analgesic activity (13) and found to be equipotent to standard drug (Aspirin25mg/ kg.)

Anti-inflammatory activity: Poultice of leaves is beneficial in glandular swellings. The root extract exhibited significant anti-inflammatory activity in Carrageen induced rat paw edema (14).

Antipyretic activity: The antipyretic activity of ethanolic, petroleum ether, solvent ether and ethyl acetate extracts of seeds was screened using yeast induced hyperpyrexia method. Paracetamol I.P (200mg/kg) was used as standard for comparison. The ethanolic and ethyl acetate extracts of seeds showed significant antipyretic activity in rats (15).

Wound healing properties: Three wound models wiz excision wound, incision wound and dead space wound were selected for assessing wound healing activity of ethanolic and ethyl acetate extracts of leaves. Ethanolic and Ethyl acetate extracts (10% w/w extract in the form of ointment) showed significant wound healing activity that is comparable with the standard vicco turmeric cream (Vicco Laboratories). Phytosterols and phenolic compounds present in these extracts promote the wound healing activity (15).

Anti asthmatic activity: A study was carried out to investigate the efficacy and safety of seed kernels of *Moringa oleifera* in the treatment of bronchial asthma. The results showed an appreciable decrease in severity of symptoms of asthma and also simultaneous improvement in respiratory tract functions (16).

Antidiabetic activity: An extract from the *Moringa* leaf has been shown to be effective in lowering blood sugar levels within 3 hours ingestion, though less effectively than the standard hypoglycaemic drug, glibenclamide (17).

Hepatoprotective activity: The methanolic and chloroform extracts of leaves of *Moringa oleifera* have shown very significant hepatoprotection against carbon tetrachloride induced hepatotoxicity in albino rats in reducing serum total bilirubin, direct bilirubin, Serum glutamic pyruvic transaminase(SGPT), and serum glutamic oxaloacetic transaminase(SGOT) levels. *Moringa* roots have been reported to possess hepatoprotective activity. The aqueous and alcoholic extracts from *Moringa* flowers were also found as hepatoprotective effect, due to the presence of quercetin, a well known flavonoid (18).

Antitumor and anticancer activity: Some isolated bioactive compounds from the seeds of *Moringa oleifera* were tested for antitumor promoting activity using 7, 12-dimethylbenzanthracene (DMBA) as initiator and 12-O-tetra-decanoyl-phorbol-13-acetate (TPA) as tumour promoter. Niazimicin, a thiocarbamate from the leaves of *Moringa oleifera* was found to be a potent chemo preventive agent in chemical carcinogenesis (19). The seed extracts have also been found to be effective on hepatic carcinogen metabolizing enzymes, antioxidant parameters and skin papilloma genesis in mice. A seed ointment had similar effect to neomycin against *Staphylococcus aureus pyoderma* in mice. It has been found that niazimicin exhibits inhibition of tumour promoter induced Epstein - Barr virus activation (20, 21).

Antimicrobial activity: *Moringa* roots are reported to be rich powerful antibacterial and antifungal effects. The root extract also showed antimicrobial property due to the presence of 4 alpha-L-rhamnosyl oxy benzyl isothiocyanate. In in-vitro experiment, MIC of *M. oleifera* showed for *Mycobacterium phlei and Bacillus subtilis* is 40 µmol/L for and 56 µmol/L respectively (22). An aqueous extract made from seeds was found to be effective against *P. aeruginosa, S.aureus and E.coli.* An extract from leaves was found to be effective at inhibiting the growth of fungi *Basidiobolus haptosporus, B. ranarums and Spirochin* found in root, is effective against both Gram positive and Gram negative bacteria. *M. oleifera* root contains Anthonine was found highly toxic to the cholera bacterium (23). The antimicrobial activity of different *Moringa oleifera* seeds extracts were tested against *Scenedesmus obliquus* (green algae), *Escherichia coli (*ATCC 13706), *Pseudomonas aeruginosa (*ATCC10145), *Staphylococcus aureus (*NAMRU 325923), *Bacillus sterothermophilus* (bacterial strains) and *Herpes Simplex* virus type 1 (HSV 1) and Polio virus type 1 (sabin vaccine). Although, *P. aeruginosa* was more resistant to all *M. oleifera extracts, B.sterothermophilus* was more sensitive than other organisms to all extracts. The effect of aqueous methanolic extract and fixed oil on HSV1 was highly similar, 52.22% and 45.20% (24).

Antihypertensive, diuretic and cholesterol lowering activities: Moringa leaf juice is known to have a stabilizing effect on blood pressure. Nitrile, mustard oil glycosides and thiocarbamate glycosides have been isolated from *Moringa* leaves which were found to be responsible for the blood pressure lowering effect (20). *Moringa* roots, leaves, flowers, gum and the aqueous infusion of seeds have been found to possess diuretic activity (25). The crude extract of *Moringa* leaves has a significant cholesterol lowering action in the blood serum of high fat diet fed rats which might be attributed to the presence of a bioactive phytoconstituent i.e. β-sitosterol (26).

Antispasmodic, Antiulcer and Anthelmintic activities: *Moringa* roots and leaves have been reported to possess antispasmodic activity. This activity of leaves has been attributed to the presence of 4 alpha-L-rhamnosyl oxy benzyl-o-methyl thiocarbamate possibly through calcium channel blocker. The spasmolytic activity exhibited by different constituents provides pharmacological basis for traditional uses of this plant in gastrointestinal motility disorder (27). The methanolic extract was found to possess significant protective actions in acetylsalicylic acid; serotonin and indomethacin induced gastric lesions in experimental rats. A significant enhancement of the healing process in acetic acid-induced chronic gastric lesions was also observed

with the extract-treated animals (28). The flower and leaves also are considered to be of high medicinal value with antihelmentic activity (29).

In blindness and eye infections: Though there are many causes of blindness, Vitamin A deficiency causes impaired dark adaption and night blindness. Eating *Moringa* leaves, pods and leaf powder which contain high proportion of Vitamin A can help to prevent night blindness and eye problems in children. Ingesting drumstick leaves (β-carotene and leutin) with oil helps in improving Vitamin A nutrition and perhaps delays the onset of cataract (30). Also the juice can be instilled into eyes in cases of conjunctivitis.

Cardiac and circulatory stimulant: All parts of the tree are reported to be used as cardiac and circulatory stimulant. Moringinine acts on the sympathetic nervous system and acts as a cardiac stimulant (31).

Antioxidant activity: Antioxidant activity reported in oil from the dried seeds is higher than BHT (Butylated Hydroxy Toluene) and alpha-tocopherol. Aqueous methanol (80%) and ethanol (70%) extracts of freeze dried leaves showed radical scavenging and antioxidant activities. The drumstick leaves are found to be a potential source of natural antioxidants (32, 33).

Antifertility activity: The aqueous extract of root and bark at a dose of 200mg/kg and 400mg/kg, respectively showed post-coital anti fertility effect in rat and also induced foetal resorption at late pregnancy (34). An aqueous extract of *Moringa oleifera* roots was investigated for its estrogenic, anti-estrogenic, progestational and anti -progestational activities. Doses up to 600 mg/kg of the extract orally failed to induce a deciduas response in the traumatized uterus of ovariectomized rats. The antifertility effect of the extract appears to be due to multiple attributes (35).

Pharmaceutical Application

Gelling agent: A study was carried out to find the gelling potential of gum exudates from the stem of *Moringa oleifera*. Diclofenac sodium gels were formulated with concentration of mucilage ranging from 5.5 to 8.5%w/w. Better gel characteristics were observed at the concentration of 8%w/w. As the pH of the gum is below 5.77 and the viscosity of the formulation (8.5%w/w) is 4.6x106cps, it is ideal for topical application (36).

Suspending agent: A comparative study of gums of *Moringa oleifera* and tracaganth was reported. Zinc oxide suspensions were prepared with gum of *Moringa oleifera* and tracaganth. Their sedimentation profile, redispersibility, degree of flocculation and rheological behaviour were compared. The results revealed that the suspending properties of *Moringa oleifera* gum are comparable with that of gum tragacanth (37).

Surfactant behavior: A study on interfacial properties and fluorescence of a coagulating protein extracted from *Moringa* seeds and its interaction with sodium dodecyl sulphate (SDS) was carried out. The study reported that; a) the protein extracted from *Moringa* seeds has significant surfactant behavior; b) the coagulant protein interacts strongly with SDS and the protein might have specific binding sites for SDS; c) there is formation of protein-SDS complex (38).

Film forming property: Studies reported that gum of *M. oleifera* has enormous potential for use in the preparation of polymeric films as drug delivery systems. The films prepared using gum of *Moringa oleifera* (5 parts of 10% w/w of mucilage of gum of *Moringa oleifera* with different proportion of plasticizers) were evaluated for parameters like water uptake, tensile strength, folding endurance and water vapour transmission rate. The films were found to be comparable with films made from other polymers and in terms of above parameters therefore the gum can be used for preparing polymeric drug delivery systems and as a film coating agent in tablets as it has low vapour transmission rate and satisfactory tensile strength (39).

As stabilizer: Plant phenolics have gained considerable interest in recent years for their potential effects against food related microorganisms. Phenolic extract obtained from the leaves of *M. oleifera* & *M. orusindica* showed stabilizing activity. In the present study effect of addition of phenolic extract from leaves of *M. oleifera* and *M. indica* on the shelf life of pineapple juice stored at 4^{0} C was investigated by monitoring the changes in titrable acidity and sensory parameters for 8 weeks. Results observed that the extracts of natural phenolics can be used to improve the quality and safety of foods (40).

Cosmetic use: Various parts of *Moringa oleifera* have cosmetic value. Cognis Laboratories Serobiologics team developed Puricare ™ and Purisoft ™, two active ingredients based on botanical peptides from the seeds of *Moringa oleifera* tree that purify hair and skin and offer protection against the effects of pollution (41). *Moringa* seed oil, known as Behen oil is widely used as a carrier oil in cosmetic preparations. The healing properties of *Moringa* oil were documented by ancient cultures. *Moringa* oil possesses exceptional oxidative stability which may explain why the Egyptians placed vases of *Moringa* oil in their tombs. It is high in oleic acid and similar in

composition to olive oil. *Moringa* oil is light and spreads easily on the skin. It is good oil for use in massage and aromatherapy applications. It can be used in body and hair care as a moisturizer and skin conditioner. Other uses include soap making and for use in cosmetic preparations such as lip balm and creams (42*). Moringa oleifera* butter, a semisolid fraction of *Moringa* oil, is used in baby products to contribute a free radical resistant emollient with exceptionally long lasting skin soften.

Detoxification/water purification: *Moringa* has the ability to remove hazardous materials from water. After oil extraction of *Moringa* seeds the left press cake contains water soluble proteins that act as effective coagulants for water purification. The charged protein molecules can serve as nontoxic natural polypeptides to settle mineral particles and organics in the purification of drinking water, vegetable oil, depositing juice and beer. *Moringa* seeds showed similar coagulation effects to alum. It is also reported that a recombinant protein in the seed is able to flocculate gram positive and gram negative bacterial cells. *Moringa* seeds could be used as a biosorbant for the removal of cadmium from aqueous media. Thus water purifying attributes of *Moringa* seeds are as coagulant, microbial elimination and as a biosorbant (43).

GUAR GUM

Guar gum is one of the outstanding representatives of that new generation of plant gums. Its source is an annual pod-bearing, drought resistant plant, called Guar, or cluster bean (*Cyamopsiste tragonolobuos C. psoraloides*) belonging to the family Leguminosae. It has been grown for several thousand years in India and Pakistan as a vegetable, and a forage crop. The guar plant is about 0.6 m high, and resembles soyabean plant in general appearance, and in its characteristic arrangement of pods along the vertical stem. The pods are 5-12.5 cm long and contain on the average 5-6 round, light brown seeds (44, 45). The guar gum molecule is a linear, or highly an iso dimensional carbohydrate polymer with a molecular weight of the order of 2200 00 (46). It is composed basically of a straight chain of D-mannose units, linked together by 1-4 glycoside linkages, and having on approximately every alternate mannose single D-galactose unit ,joined to it by an a (1-6) glycoside linkage. This polysaccharide is representative of a group of galactomannan gums obtainable from many of the Leguminosae plants seeds where they serve as food reserve for e.g. Alfalfa, clover, fenugreek and, the best known locust bean (47-49).

General Properties of Guar Gum

It is white to yellowish-white, nearly odourless, free-flowing powder. It is stable in solutions over a wide range of pH values from 2-10. It is used as an effective binder, emulsifier, stabilizer, thickener, additive and suspending agent in paper, food, pharmaceutical and cosmetics industry. It is compatible with many other hydrocolloids used in food formulations. It is also used in bakeries, diaries, in dressings and sauces. Guar is an important natural food supplement with high nutritional value, promoting weight gain and cholesterol reduction. It improves immune function. It has hypoglycaemic and cholesterol-lowering action.

Pharmacological Use

Hypoglycaemic Effect: GG has been reported to attenuate postprandial glycaemia (50, 51, 52) and attenuate the fall in blood pressure of type 2 diabetes patients after oral glucose (53). Serum insulin concentrations are also decreased (54, 55, 56). Physicochemical characteristics of GG in the upper intestine may be important in determining blood glucose level. PHGG, which is low in molecular weight and viscosity, has been reported to significantly decrease serum cholesterol, free fatty acid and glucose concentrations when administered to healthy young adults at 15 g/d, but the decrease was not significant when the dosage was 5 g/d (57).

Hypolipidemic agent: Guar gum is a dietary fibre advocated for use in lowering serum total cholesterol levels in patients with hypercholesterolemia. Its mechanism of action is proposed to be similar to that of the bile-sequestering resins. Although guar gum is also employed as an adjunct in non-insulin-dependent diabetic patients this review is restricted to its efficacy as a hypolipidaemic agent. Clinical trials indicate that, when used alone, guar gum may reduce serum total cholesterol by 10 to 15%. As an adjunct to established therapies (Bezafibrate, Lovastatin or Gemfibrozil) guar gum has shown some promise: it may produce a further reduction in total cholesterol of about 10% in patients not responding adequately to these drugs alone. Thus, on the basis of presently available evidence guar gum as monotherapy may be considered at most modestly effective in reducing serum cholesterol levels (58, 59).

Both GG and PHGG have been reported to significantly depress plasma and serum triglycerides, triglyceride-rich lipoprotein, total cholesterol, and a lipoprotein E level. Increased bile acid excretion seems to be essential in

the cholesterol-lowering effect of soluble fibers and related compounds. This effect is connected to induction of HMG CoA reductase and lowering concentrations of a lipoprotein E-containing particle (60).

The role of intestinal viscosity on the cholesterol-lowering effect of dietary fiber by comparing the cholesterol-effect of intact GG and PHGG was studied. Compared with the low viscosity PHGG diet, the high viscosity intact GG diet was more potent in enhancing bile acid excretion and producing a potent cholesterol-lowering effect. Both PHGG and GG depressed plasma triglycerides whereas only the GG depressed low-density lipoprotein (LDL). The decreased efficiency of the PHGG diet to produce a hypocholesterolemic response resulted in a decreased stimulation of hydroxyl methyl glutaryl coenzyme A (HMG CoA) reductase, and this could explain the lesser efficiency of the PHGG diet to develop a cholesterol-lowering effect (61).

The hypocholesterolemic effect of dietary fibers might also be mediated by the SCFA from fiber fermentation. Propionate is reported to inhibit fatty acid metabolism which plays a key role in the synthesis of cholesterol. Propionic acid has been reported to inhibit hepatic lipogenesis from acetate (62).

Improved Immune Function: Yamada et al. (1999) compared the effect of dietary GG (Guar Gum) or PHGG (Partially Hydrolyzed Guar Gum) on the serum lipid level and immunoglobulin (Ig) production of Sprague-Dawley rats with that of water-insoluble cellulose. Both GG and PHGG feeding enhanced IgA productivity in the spleen and mesenteric lymph node lymphocytes, and an increase in serum IgA level was observed in the rats fed GG but not PHGG(63).

In a similar study by the same group (Yamada et al., 2003), the IgA and IgG productivity in mesenteric lymph node (MLN) lymphocytes was significantly higher in the rats fed GG than in those fed cellulose. In addition, GG induced a significant increase of IgM productivity in MLN lymphocytes when compared to the cellulose group. GG, as a polysaccharide of galactomannan, may also enhance macrophage activities (64). A high-molecular-weight galactomannan, about 1.0 million Daltons, isolated from the edible mushroom *Morchellaesculenta*, was demonstrated to enhance macrophage activation thus exhibiting immune stimulatory activity (Duncan et al., 2002)(65).

Inhibition of Colonic Cancer and Improved Colon Health: The health of the large intestine and colon is paramount because they, in addition to serving as a primary site for water re-absorption, play an important role as a major immune organ and function as a barrier to prevent foreign materials from dietary or microbial origin from crossing into the internal body cavity. Heitman et al. (1992), (66) reported that dietary supplementation with 10% GG (fed during the promotional stage of carcinogenesis) was found to suppress colon cancer incidence to a significant extent. The SCFA produced by colonic microbes with the substrate of soluble fibers has been proposed to play a key role in enhancing colon health by both stimulating cell division and regulating apoptosis (Wasan and Good lad, 1996) (67).Butyrate has been shown to increase apoptosis in human colonic tumor cell lines (Brouns et al., 2002). Apoptosis is a mechanism where excess or redundant cells are removed during development and restricted tissue size is maintained, thus serving as an innate cellular defence against carcinogenesis. Reduced intestinal pH by SCFA has a direct impact on carcinogenesis in the large intestine (Tungland and Meyer, 2002(68). Lowered colonic pH affects pH-dependent enzymatic reactions, for example, secondary bile acid formation. SCFA can also decrease the amount of pathogenic bacteria in colon which results in a reduction in the production of carcinogenic substances. Dietary fiber could also reduce the amount of carcinogenic substances available to colonic mucosa by adsorption of the substances to the cell walls of the micro biota, by speeding up the intestinal transit time and by increasing colonic contents and thus diluting all solutes.

Improved Mineral Bioavailability: The effect of PHGG and intact GG on iron utilization in rats fed several iron-deficient diets was studied and it was found that the haemoglobin, serum iron and iron storage in the liver of rats fed iron-deficient diets as a control group (without PHGG and GG) significantly decreased, while those of the test group fed together with PHGG or GG were unchanged (69). In an iron balance test for 3 d, administration of PHGG or GG caused an increase in iron absorption. These results suggested that PHGG and GG increase the bioavailability of dietary iron in deficiency.

In studying the effect of dietary FF on mineral excretion of young male rats (70) it was found that dietary inclusion of GG significantly decreased fecal excretion of Ca, P, Mg, and Cu, and increased serum, but not bone, levels of these minerals with exception of P. Through their fermentation by colonic microbes and subsequent SCFA production, dietary fibers stimulate the proliferation of epithelial cells in the cacao-colon and reduce the luminal pH. The SCFA and lower pH may, in turn, dissolve insoluble mineral salts, especially calcium, magnesium and iron in the luminal content and increase their diffusive absorption via the paracellular route.

Pharmaceutical Applications:

Colon targeted drug delivery: A novel formulation consisting of cross-linked microspheres of guar gum has been investigated for colon-targeted delivery of metronidazole. An emulsification method involving the dispersion of aqueous solution of guar gum in castor oil was used to prepare spherical microspheres. Process parameters were analyzed in order to optimize the formulation. Shape and surface morphology of the microspheres were examined using scanning electron microscopy. Placebo microspheres exhibited a smooth surface while the incorporation of drug imparted a slight roughness to the surface texture. Particle size of the microspheres was determined using laser diffraction particle size analyzer. The in vitro drug release studies were performed in simulated gastric fluid for 2 h and intestinal fluid for 3 h, which revealed that the drug was retained comfortably inside the microspheres and that only 15.27+/-0.56% of the drug was released in 5 h. In vitro release rate studies were also carried out in simulated colonic fluid (SCF) in the presence of rat cecal contents, which showed improved drug release. Moreover, to induce the enzymes that specifically act on guar gum, the rats were treated with 1 ml of 1% w/v dispersion of guar gum for 2, 4 and 6 days and release rate studies were repeated in SCF in the presence of 2 and 4% w/v of cecal matter. A marked improvement in the drug release was observed in presence of cecal matter obtained after induction when compared to those without induction. In vitro release studies exhibited 31.23+/-1.49% drug release in 24 h in dissolution medium without rat cecal matter. However, the incorporation of 4% w/v cecal matter obtained after 6 days of enzymes induction increased the drug release to 96.24+/-4.77% (71).

Oral controlled drug delivery: The objective of the study was to develop guar gum matrix tablets for oral controlled release of water-soluble diltiazem hydrochloride. Matrix tablets of diltiazem hydrochloride, using various viscosity grades of guar gum in 2 proportions, were prepared by wet granulation method and subjected to in vitro drug release studies. Diltiazem hydrochloride matrix tablets containing either 30% wt/wt low viscosity (LM1), 40% wt/wt medium-viscosity (MM2), or 50% wt/wt high-viscosity (HM2) guar gum showed controlled release. The drug release from all guar gum matrix tablets followed first-order kinetics via Fickian-diffusion. Further, the results of in vitro drug release studies in simulated gastrointestinal and colonic fluids showed that HM2 tablets provided controlled release comparable with marketed sustained release diltiazem hydrochloride tablets (D-SR tablets). Guar gum matrix tablets HM2 showed no change in physical appearance, drug content, or in dissolution pattern after storage at 40 ^{0}C/relative humidity 75% for 6 months. When subjected to in vivo pharmacokinetic evaluation in healthy volunteers, the HM2 tablets provided a slow and prolonged drug release when compared with D-SR tablets. Based on the results of in vitro and in vivo studies it was concluded that that guar gum matrix tablets provided oral controlled release of water-soluble diltiazem hydrochloride (72).

Ocimum basilicum

Ocimum basilicum usually named common basil or sweet basil is an annual plant, with extraordinary medicinal properties and contains several antioxidant compounds. Sweet basil is native to tropical Asia. It is cultivated commercially in southern Europe, Egypt, Morocco, Indonesia and California. Basil is an annual herb to 2-3 ft (0.6-0.9 m) tall with green stems (usually woody at the base) that are square in cross section. Basil has opposite leaves, 2-4 inch (5.1-10.2cm) long, and tiny purple or white flowers arranged in flattened whorls that encircle the stems, one whorl above another. Plants are leafy and branch freely with a pair of opposing branches in a flat plane, then another pair above in a plane perpendicular to the last, and so on. There are many cultivars of basil, selected for their fragrances and colour.

In traditional medicine, *Ocimum basilicum* has been used as an antiseptic, preservative, sedative, digestive regulator and diuretic. It also has been recommended for the treatment of headaches, coughs, infections of upper respiratory tract, kidney mal function and to eliminate toxins.

Pharmacological Applications:

Anti-hyperglycaemic and Hypolipidemic Effects: The hypoglycaemic and hypolipidemic effects of the aqueous extract of *Ocimum basilicum* (OB) whole plant were investigated in normal and streptozotocin (STZ) diabetic rats. After a single oral administration, OB significantly reduced blood glucose levels in normal ($p<0.01$) and diabetic rats ($p<0.001$). After 15 days of repeated oral administration, OB produced a potent reduction of blood glucose levels ($p<0.001$) in diabetic rats and a less reduction in normal rats ($p<0.05$). Total plasma cholesterol and triglycerides levels were significantly reduced after repeated oral administration in diabetic rats ($p<0.001$) and ($p<0.05$) respectively. However, no change was observed in total plasma cholesterol

and triglycerides levels in normal rats after both single and repeated oral administration. In addition, plasma insulin levels and body weight remained unchanged over 15 days of oral administration in normal and diabetic rats. We conclude that the aqueous extract of OB exhibits potent anti-hyperglycaemic and hypolipidemic activities in diabetic rats without affecting basal plasma insulin concentrations (73).

Antigiardial activity: In this study, the effects of *Ocimum basilicum* essential oil on Giardia lamblia and on the modulation of the interaction of these parasites by peritoneal mouse macrophage have been investigated. The essential oil (2 mg/ml) and its purified substances demonstrated antigiardial activity. Linalool (300 µg/ml), however, was able to kill 100% parasites after 1 h of incubation, which demonstrates its high antigiardial potential. Pre treatment of peritoneal mouse macrophages with 2 mg/ml essential oil dilution reduced in 79% the association index between these macrophages and G. lamblia, with a concomitant increase by 153% on nitric oxide production by the G. lamblia-ingested macrophages. The protein profiles and proteolitic activity of these parasite trophozoites, previously treated or not with 2 mg/ml essential oil or with the purified fractions were also determined. After 1 and 2 h of incubation, proteins of lysates and culture supernatants revealed significant differences in bands patterns when compared to controls. Besides, the proteolitic activity, mainly of cysteine proteases, was clearly inhibited by the essential oil (2 mg/ml) and the purified linalool (300µg/ml). These results suggest that, with G. lamblia, the essential oil from *O. basilicum* and its purified compounds, especially linalool, have a potent antimicrobial activity (74).

Antioxidant Activity: The present study was carried out to evaluate the *in-vitro* antioxidant activities of 50% hydro alcoholic extract of Ocimum species namely *Ocimum basilicum* and *Ocimum sanctum* .This was achieved by screening the two plant extracts at varying concentrations (10-5µg/ml) using DPPH radical scavenging activity, reducing power assay, hydroxyl radical scavenging activity and nitric oxide radical scavenging activity. The results were analyzed statistically which showed that *Ocimum basilicum* had more antioxidant activity than *Ocimum sanctum* (75).

Antimicrobial Activity: Ethanol, methanol, and hexane extracts from *Ocimum basilicum* (sweet basil) were investigated for their in-vitro antimicrobial properties. A total of 146 microbial organisms belonging to 55 bacteria, and four fungi, and a yeast species were studied using a disk-diffusion and minimal inhibition concentration (MIC) method. The result showed that none of the three extracts tested have antifungal activities, but anti candidal and antibacterial effects. Both the hexane and methanol extracts, but not the ethanol extracts, inhibited three isolates out of 23 strains of Candida albicans studied. All three extract of *O. basilicum* were different in terms of their antibacterial activities. The hexane extract showed a stronger and broader spectrum of antibacterial activity, followed by the methanol and ethanol extracts, which inhibited 10, 9 and 6% of the 146 bacterial strains tested, respectively. The minimal inhibition zones (MIC) of the hexane, methanol, and ethanol extracts ranged from 125 to 250 µl/ml, 62.50 to 500 µl/ml, and 125 to 250 µl/ml respectively (76).

Cardiac stimulant activity: The aerial parts of *Ocimum basilicum* were extracted with ethanol & double distilled water. The extracts were screened for their effects on frog in situ heart preparation. Enzymes studies such as Na/k ATPase, Ca ATPase & Mg ATPase were done on heart tissue .AST, ALT; LDH & CPK were estimated in heart tissue& serum of albino rats after administering the extracts for seven days. The alcoholic extracts produce a cardio tonic effect & aqueous extract produce a β-adrenergic effect (77).

Pharmaceutical Applications:

Granulating and binding agent: study elucidate and quantify the compressibility and compactibility of herbal granules prepared by using hydrogel isolated from whole seeds of *Ocimum basilicum* as a novel binder. The compressibility is the ability of the powder to deform under pressure and the compactibility is the ability of a powder to form coherent compacts. To test the functionality of novel excipients, Sonnergaard proved a simple linear model to confirm compatibility, which is an uncomplicated tool for quantification. The tablets were compressed at increasing compression pressures and were evaluated for various mechanical properties. The linear relationship between specific crushing strength and compression pressure revealed the compactibility of the herbal granules and the linear relationship between porosity and logarithm of compression pressure revealed the compressible nature of the herbal granules according to the model developed by Sonnergaard. Thus the hydrogel isolated from whole seeds of *Ocimum basillicum* had potential as a granulating and binding agent (78).

Disintegrating agent: Ibuprofen dispersible tablets using Plantago ovata mucilage powder, *Ocimum basilicum* mucilage powder, Plantago ovata husk powder and *Ocimum basilicum* seed powder as disintegrants were prepared and disintegrating property was studied. The swelling index of the above disintegrants was studied. Disintegrating property of the above disintegrants was evaluated by comparing with the formulations of starch powder as standard disintegrant. The study revealed that *Plantago ovata* seed powder and mucilage powder

were effective in low concentrations (5%) as disintegrants compared to others. The study further revealed a poor relation between the swelling index and disintegrating efficiency (79).

COPAL GUM

Gum copal is a natural resinous material of plant *Bursera bipinnata*, family Burseraceae. Copal, a resinous material, is obtained from the plants of araucariaceae and caesalpinaceae, a subfamily of leguminoceae. Copal resin (CR) contains agathic acid, a diterpenoid and related lobdane compounds along with cis-communic acid, trans-communic acid, polycommunic acid, sandaracccopimaric acid, agathalic acid, monomethyl ester of agathalic acid, agatholic acid and acetoxyagatholic acid CR obtained from leguminoceae family contains copalic acid, pimaric acid, isopimaric acid, dehydro-dehydroabietic acid,

Dehydro abietic acid and abietic acid (80, 81).

Pharmacological Applications:

Copal is also used in the treatment of headache, fever, burns and stomach ache (82). It also acts as binding media in dental products and in treatment of micro leakage in teeth (83).

Pharmaceutical Applications:

Sustained drug delivery & colon targeted drug delivery: Copal resin (CR) was investigated for its physicochemical properties, which are yellowish cream in colour with acid value 129.82 ± 2.38, saponification value 172.60 ± 4.03, ester value 42.78 ± 3.19, softening point 88-92°C, glass transition temperature (Tg) 85.29°C, refractive index 1.534-1.536 and moisture content (loss on drying) 0.699 ± 0.08% w/w. The free films, prepared in alcohol by solvent evaporation technique, were brittle with high tacking property. Addition of 1% w/w propylene glycol improved the mechanical properties (tensile strength, percent elongation and Young's modulus) of CR films, whereas glyceryl monostearate, sorbitan mono-oleate and Sorbitan mono laurate in 15% w/w reduced the tackiness significantly. Water vapour transmission rate of CR film was $2.16 \pm 0.31 \times 10^{-5}$ g cm/cm^2 and $4.13 \pm 0.18 \times 10^{-5}$ g cm/cm^2 at relative humidity (RH) of 43% and 93%, respectively. CR films show good swelling property in phosphate buffer (pH 7.4). Present investigation proposes the film-forming natural material with its potential as a coating material for sustained release and colon-targeted drug delivery (84, 85).

DAMMARGUM

Dammar gum is obtained from the Dipterocarpaceae family of trees in India and East Asia, principally those of the genera Shorea, Balanocarpus, or Hopea. Gum dammar (GD) is a natural gum of plant *Shorea wiesneri* (family Dipterocarpaceae). It contains about 40% α-resin, 22% β- resin, 23% dammarol acid and 2.5% water. Most is produced by tapping trees; however some is collected in fossilized form from the ground. The gum varies in colour from clear to pale yellow, while the fossilized form is grey-brown. It is used in foods, as either a clouding or a glazing agent, in the making of incense, varnishing and in other processes. Dammar was first introduced as a picture varnish in 1826 and is commonly referred to as Dammar varnish. Dammar varnish is commonly used in oil painting, both during the painting process and after the painting is finished. The name is a Malay word meaning "*resin*" or "*torch made from resin*"(86,87,88,89).

There are two further types of Dammar, besides the gum:

"*Mata kucing*" ("*cat's eye*") is a crystalline resin usually in the form of round balls.

"*Batu*" ("*stone*") is the name given to the stone or pebble-shaped opaque dammar collected from the ground (89).

Pharmacological Applications:

It is utilized to combat sadness, depression and melancholy (90).

Pharmaceutical Applications:

Microencapsulating agent: Gum dammar was investigated as a novel microencapsulating material for sustained drug delivery. Microparticles were prepared by oil-in-oil emulsion solvent evaporation method. Ibuprofen and diltiazem hydrochloride were used as model drugs. Microparticles were evaluated for particle size, encapsulation efficiency and in vitro drug release kinetics. Images of the microparticles were obtained by

bright field microscopy. The effect of different gum: drug ratios and solubility of drug on micro particle properties was principally investigated. Gum dammar could produce discrete and spherical microparticles with both drugs. With a freely water soluble drug (diltiazem hydrochloride), gum dammar produced bigger (45-50 µm) and fast drug releasing microparticles with low encapsulation efficiencies (44-57%). Contrary, with a slightly water soluble drug (ibuprofen), gum dammar produced small (24-33 µm) microparticles with better drug encapsulation (85-91%) and sustained drug delivery. The increase in gum: drug ratio showed an increase in particle size, encapsulation efficiency and decrease in drug release rate in all cases. Drug release profiles of all microparticles followed zero order kinetics. In conclusion, gum damar can be used successfully to produce discrete and spherical microparticles of ibuprofen and diltiazem hydrochloride (91).

TAMARIND

Tamarind *(Tamarindus Indica L.)* is amongst the most common and commercially important, large evergreen tree that grows abundantly in dry tracks of central and south Indian states, also in other south east-asian countries. The pulpy portion of fruit is mainly used as acidulent in Indian recipes. Tamarind seeds or kernel is a by product of Tamarind pulp industry. Tamarind gum is obtained from endosperm of seeds of the tamarind tree, which is a seed gum with potential industrial applications. Tamarind gum or tamarind kernel powder came into commercial production in 1943 as a replacement for starch in cotton sizing in Indian textile market. It is also used in microbial production of lipids (92, 93, 94). It is an important sizing material for textile, a good creaming agent for concentration of rubber latex used as a soil stabilizer, a rich source of proteins and amino acids (95). Moreover tamarind kernel powder may also be used as a feed for cattle and pigs (96). It is also used as food ingredient. Currently purified and refined tamarind kernel powder is produced and permitted in Japan as a thickening, stabilizing and gelling agent in the food industry (97).Gum solution of good adhesive strength from tamarind gum and sisal fibers were prepared which have potential industrial applications such as for false roofing and room portioning (98). Tamarind gum is used as a creamer for latex, in explosives, in borax printing and paper manufacturing. It is also used as stabilizer in ice creams and as an emulsion textile paste (99). Thus tamarind gum is having applications in paper, food, textile industry etc. Recent year's research has been initiated on the use of tamarind gum in pharmaceutical and cosmetic applications.

Chemical composition:

The composition of tamarind kernel, the source of gum, resembles the cereals. With 15.4 % to 12.7 % protein, 3-7.5 % oil, 7-8.2 % crude fiber, 61-72.2 % non fiber carbohydrates, 2.45-3.3 % ash; all were measured on a dry basis. Chemically tamarind kernel powder is highly branched carbohydrate polymer. Its backbone consists of D-glucose units joined with (1-4) β-linkages similar to that of cellulose. It consists of a main chain of β-D- (1-4)-galactopyranosyl unit with a side chain of single xylopyranosyl unit attached to every second, third and fourth of D-glucopyranosyl unit through α-D- (1-6) linkage. One galactopyranosyl unit is attached to one of the xylopyranosyl units through β-D- (1-2) linkage. The exact sequential distribution of branches along the main chain is uncertain (100,101).

Physical properties:

Tamarind kernel powder disperses and hydrates quickly in cold water but does not reach maximum viscosity unless it is heated for 20-30 mins. The solution exhibits typical non Newtonian flow properties common to most other hydrocolloids. The functional properties of tamarind kernel powder of protein concentrates were reported. The rheological properties of tamarind kernel powder suspension showed that suspension behaved like non Newtonian, pseudo plastic fluid with yield stresses and exhibited thixotropic characteristics. An increasing concentration produces increase in non Newtonian behavior as in consistency latex, yields stress and apparent viscosity (102-104).

Pharmaceutical Applications:

Dissolution improvement

Tamarind kernel powder is evaluated for its suitability as a carrier to improve the dissolution rate of poorly water-soluble drug Celecoxib. Influence of polysaccharide concentration and method of preparation of solid mixtures on dissolution rates was investigated. Order of dissolution efficiencies was found to be solvent deposition > co-grinding> kneading > physical mixing > pure Celecoxib (105).

Nasal Mucoadhesion

Tamarind gum along with xanthan gum and hydroxypropyl cellulose (water soluble neutral polymer) used for nasal mucoadhesion studies in powder formulation. Result of this study suggested that the residence time of drug in nasal cavity may be prolonged by using hydroxypropyl cellulose, xanthan gum and tamarind gum as a base for powder preparation of intranasal administration and residence time may be controlled by mixing two or more polymers differing in Mucoadhesion (106).

Bioadhesive Tablet

Tamarind gum was also evaluated in bio adhesive tablets. It was showed that lactoferrin tablet prepared with tamarind gum showed longest residence time in oral cavity as compared with xanthan gum and carboxymethyl cellulose but an unpleasant taste gradually developed (107).

Tamarind seed polysaccharide:

Polysaccharide present in tamarind kernel powder is called as tamarind seed polysaccharide. Tamarind seed polysaccharide is having molecular weight 52350 units and monomer of glucose, galactose and xylose in molar ratio of 3:1:2 (108). Various methods have been reported for isolation of tamarind seed polysaccharide from tamarind kernel powder. It is insoluble in organic solvents and dispersible in hot water to form a highly viscous gel such as mucilaginous solutions with a broad pH tolerance and adhesivity. In addition it is nontoxic and non irritant with haemostatic activity (109,110). Recently tamarind seed polysaccharide is widely used for pharmaceutical applications.

Pharmaceutical Applications of Tamarind Seed Polysaccharide:

Binder in tablet dosage form

Evaluations of tamarind seed polyose as a binder for tablet dosage forms was taken up for the wet granulation as well as direct compression methods. The results indicated that tamarind seed polyose could be used as binder for wet granulation and direct compression tableting methods (111,112).

In Ophthalmic drug delivery

Tamarind seed polysaccharide is used for production of thickened ophthalmic solutions having a pseudo plastic rheological behaviour and mucoadhesive properties. Said solution is used as artificial tear and as a vehicle for sustained release ophthalmic drugs. The concentrations of tamarind seed polysaccharide preferably employed in ophthalmic preparations for use as artificial tears i.e. a products for replacing and stabilizing the natural tear fluid, particularly indicated for the treatment of eye syndrome are comprised between 0.7-1.5 percent by weight. The concentrations of tamarind polysaccharides preferably employed in the production of vehicles (i.e. delivery system) for ophthalmic drugs having the function of prolonging the prevalence time of medicaments at their site of actions are comprised between 1 and 4 % by weight (113).

In sustained drug delivery

It is used as potential polysaccharide having high drug holding capacity for sustained release of verapamil hydrochloride. The release pattern was found to be comparable with matrices of other polysaccharide polymers such as ethyl cellulose, hydroxyethyl cellulose and hydroxyl propyl methyl cellulose, as well as the commercially available sustained release tablets (isoptin SR) (114). It is also used as suitable polymer for sustained release formulations of low drug loading. Sustained release behaviours of both water soluble (acetaminophen, caffeine, theophylline and salicylic acid) and water insoluble (indomethacin) drugs on tamarind seed polysaccharide was examined (115). Studies showed that tamarind seed polysaccharide could be used for controlled release of both water-soluble and water insoluble drugs. Zero order release can be achieved taking sparingly soluble drugs like indomethacin from tamarind seed polysaccharide. The rate of release can be controlled by using suitable diluents like lactose and microcrystalline cellulose. For water-soluble drugs, the release amount can also be controlled by partially crosslinking the matrix. The extent of release can be varied by controlling the degree of cross linking. The mechanism of release due to effect of diluents was found to be anomalous and due to crosslinking was found to be super case II (116).

In Ocular drug delivery

Tamarind seed polysaccharide was used for ocular delivery of 0.3 % rufloxacin in the treatment of experimental pseudomonas aeruginosa and staphylococcus aureus keratitis in rabbits. The polysaccharide significantly increases the intraocular penetration of rufloxacin in both infected and uninfected eyes. Polysaccharide allows sustained reduction of S. aureus in cornea to be achieved even when the time interval between drug

administrations was extended. The results suggested that tamarind seed polysaccharide prolongs the pre corneal residence time of antibiotic and enhances the drug accumulation in the cornea, probably by reducing the washout of topically administered drugs (117).

In controlled release of spheroids

Tamarind seed polysaccharide was used as release modifier for the preparation of diclofenac sodium spheroids using extrusion spheronization technique with microcrystalline cellulose as spheronization enhancer. It was found that release was sustained over a period of 7.5 hour. A credible correlation was obtained amongst swelling index, viscosity, and surface roughness of the polysaccharide particles and in vitro dissolution profile of spheroids. In the comparative bioavailability study the developed spheroids have able to sustained drug release and also was found to improve the extent of absorption and bioavailability of drug (118).

CONCLUSION

After survey of various literatures I have concluded that natural polymer like *Moringa oleifera, Cyamopsiste tragonolobuos, Ocimum basilicum, Bursera bipinnata, Shorea wiesneri, Tamarindus indica* plays a vital role in the development of Novel drug delivery systems. So in future these polymers may be used widely by the researcher for the development of NDDS because of its advantage over other synthetic polymer. We anticipate that more uses of natural polymer will be coming as additional derivatives are synthesized and newer formulations are developed. The natural polymers can serve a number of purposes, including as a coating agent, gel former, controlled-release matrix, in addition to inducing desirable properties, such as mucoadhesion and permeation enhancement to improve oral bioavailability of a drug.

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