4. DRUG AND POLYMER PROFILES

4.1. Drug Profile

4.1.1. Curcumin

4.1.1.1. Source and chemical composition

Curcumin is an orange-yellow crystalline powder obtained from rhizome of Curcuma longa, family Zingiberaceae.

The three principal colouring components of curcumin that are present in various proportions are all dicinnamoylmethane derivatives: (1) 1,7-Bis-(4-hydroxy-3-methoxyphenyl)-hepta-1,6-diene-3,5 dione = diferuloyl methane (Chemical formula: C_{21}H_{20}O_{6}, Formula weight: 368). (2) 1-(4-hydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-hepta-1,6-diene-3,5dione = phydroxycinnamoyl ferulo methane (Chemical formula: C_{20}H_{18}O_{5}, Formula weight: 338). (3) 1,7-Bis-(4-hydroxyphenyl)-hepta-1,6-diene-3,5dione=p,pdihydroxy dicinnamoyl methane (Chemical formula: C_{19}H_{16}O_{4}, Formula weight: 308)\(^{114}\).

Curcumin was first isolated in 1815, obtained in crystalline form in 1870 and identified as 1,6-heptadiene-3,5-dione-1,7-bis(4-hydroxy-3-methoxyphenyl)-(1E,6E) or diferuloyl methane. The feruloylmethane skeleton of curcumin was subsequently confirmed in 1910 by the initial work and synthesis by Lampe. Curcumin is a yellow–orange powder that is insoluble in water and ether but soluble in ethanol, dimethylsulfoxide and acetone. Curcumin has a melting point of 183°C, molecular formula of C_{21}H_{20}O_{6} and molecular weight of 368.37 g/mol. Curcumin (also known as curcumin I) occurs naturally in the rhizome of Curcuma longa, which is grown commercially and sold as turmeric, a yellow–orange dye. Turmeric contains curcumin along with other chemical constituents known as the “curcuminoids”. The major curcuminoids present in turmeric are demethoxycurcumin (curcumin II), bisdemethoxycurcumin (curcumin III) and the recently identified cyclocurcumin (Fig. 4.1). Commercial curcumin contains curcumin I (~77%), curcumin II (~17%), and curcumin III (~3%) as its major components. The curcuminoid complex is also referred to as Indian saffron, yellow ginger, yellow root, kacha haldi, ukon, or natural yellow 3.
4.1.1.2. Physico-chemical properties

Curcumin is soluble in oil and alkali, practically insoluble in water, acidic and neutral pH. In solutions the principal colouring components of curcumin exhibit keto-enol tautomerism and depending on the solvent, up to 95 percent are in the enol form\(^{115}\) (Fig. 4.2).

4.1.1.3. Pharmacological properties of curcumin (Fig. 4.3).

4.1.1.3.1. Curcumin inhibits angiogenesis

Angiogenesis (blood vessel formation) is essential for tumor growth and metastasis. The precise mechanism that leads to angiogenesis is not fully understood, but growth factors that cause proliferation of endothelial cells have been shown to play a critical role in this process. Curcumin has been shown to suppress the proliferation of human vascular endothelial cells and abrogate the fibroblast growth factor-2–induced angiogenic response suggesting that curcumin have an antiangiogenic factor. CD13/aminopeptidase N (APN) is a membrane-bound, zinc
dependent metalloproteinase that plays a key role in tumor invasion and angiogenesis. Curcumin binds to APN and irreversibly inhibits its activity. Indeed curcumin has been shown to suppress angiogenesis in vivo e.g. inhibition of angiogenesis of LNCaP prostate cancer cells. To elucidate the possible mechanism of antiangiogenic activity by curcumin performed by cDNA microarray analysis and found that curcumin modulated cell-cycle–related gene expression. Specifically, curcumin induced G0/G1 and/or G2/M phase cell cycle arrest, upregulated CDKIs, p21WAF1/CIP1, p27KIP1, and p53, and slightly downregulated cyclin B1 and CDC2 in ECV304 cells. The upregulation of CDKIs by curcumin played a critical role in the regulation of cell cycle distribution which may underlie the antiangiogenic activity of curcumin.

4.1.1.3.2. Suppression of protein kinases by curcumin

Curcumin could also mediate its effects through inhibition of various other serine/threonine protein kinases. It showed that treatment of highly purified protein kinase A (PKA), protein kinase C (PKC), protamine kinase (cPK), phosphorylase kinase (PhK), autophosphorylation-activated protein kinase (AK), and pp60c-src tyrosine kinase with curcumin inhibited all kinases. PhK was completely inhibited at low concentration of curcumin. At around 0.1 mM curcumin, PhK, pp60c-src, PKC, PKA, AK, and cPK were inhibited by 98, 40, 15, 10, 1, and 0.5%, respectively. Treatment of cells with 15 or 20 μM curcumin inhibited TPA-induced PKC activity in the particulate fraction by 26 or 60%, respectively, and did not affect the level of PKC. Curcumin also inhibited PKC activity in both cytosolic and particulate fractions by competing with phosphatidylyserine. However, the inhibitory effect of curcumin was reduced after preincubation with the thiol compounds. These findings suggested that the suppression of PKC activity may contribute to the molecular mechanism of inhibition of TPA-induced tumor promotion by curcumin. Besides in vitro suppression, curcumin could also inhibit PKC in the cells. Curcumin inhibits Ca²⁺- and phospholipid-dependent PKC and of the catalytic subunit of cyclic AMP-dependent protein kinase (cAK; IC50 values 15 and 4.8 μM, respectively). Curcumin inhibits plant Ca²⁺-dependent protein kinase (CDPK) (IC50 41 μM), but does not inhibit myosin light chain kinase or a high-affinity 35’-cyclic AMP–binding phosphatase.
Figure 4.3. Pharmacological Properties of curcumin
4.1.2. Betulinic acid

4.1.2.1. Source and chemical composition

Betulinic acid (Fig. 4.1.2.1), 3β-hydroxy-lup-20(29)-en-28-oic acid is a widely distributed pentacyclic lupane-type triterpene in the plant kingdom. Considerable amounts of betulinic acid (up to 2.5%) are available in the outer bark of a variety of tree species. A closely related compound, betulin, is a major constituent of white-barked birch trees (Betula species) with yields up to 22% (dry weight). White birch bark, Betula alba (which contains betulinic acid) has been used by native Americans as a folk remedy. They used it in tea and other beverages to treat stomach and intestinal problems such as diarrhea and dysentry. In Russia, it has been reportedly used since 1834. In 1994, scientists at the University of North Carolina reported that chemicals found in white birch bark slowed the growth of human immunodeficiency virus (HIV). The following year, a researcher at the University of Illinois reported that betulinic acid killed melanoma cells in mice. Since then, a number of researchers have conducted laboratory tests on betulinic acid to determine antitumor properties, especially with respect to melanoma cells with some promising results which may warrant future study. Betulinic acid has recently been selected by the National Cancer Institute for addition into the RAID (Rapid Access to Intervention in Development) programme.116

![Fig. 4.1.2.1. Structure of betulinic acid](image-url)
4.1.2. 2. Physicochemical properties

It is white crystalline powder, pKa 5.50, practically insoluble in aqueous media, molecular weight 456.71 and melting point 295-298°C.

4.1.2. 3. Pharmacokinetics and tissue distribution

Pharmacokinetics and tissue distribution of betulinic acid in CD-1 mice showed that after i.p. 250 and 500 mg/Kg dose, the serum concentrations reached peaks at 0.15 and 0.23 h, respectively. The 250 and 500 mg/Kg betulinic acid i.p. doses were found to have elimination half-lives of 11.5 and 11.8 h and total clearances of 13.6 and 13.5 l Kg/h, respectively. The pharmacokinetic parameters observed for i.p. betulinic acid 500 mg/Kg in the skin of mice were as follows: $K_a$ (h⁻¹) 0.257, $K_{10}$ (h⁻¹) 0.234, $t_{1/2}$ (a) (h) 2.63, $t_{1/2}$ (b) (h) 20.2, $V_d$ (l/Kg) 0.61, AUC (mg/mL) 3504, $T_{max}$ (h) 3.90 and $C_{max}$ (mg/mL) 300.9. The distribution of betulinic acid in tissues at 24 h post i.p. administration in a descending order was as follows: perirenal fat (2260 mg/g), ovary (1998 mg/g), spleen (1287 mg/g), mammary gland (1184 mg), uterus (980 mg/g), and bladder, lymph node, liver, small intestine, caecum, lung, thymus, colon, kidney, skin, heart and brain (1 mg/g). Recently developed a robust assay based on liquid chromatography/mass spectrometry to conduct a quantitative analysis of betulinic acid in mouse, rat and dog plasma. At 15 and 25 mg/mL in mouse, rat or dog plasma, betulinic acid was 99.99% bound to serum proteins and at 5 mg/mL, betulinic acid was > or =99.97% bound.

4.1.2. 4. Pharmacological properties

Betulinic acid is a naturally occurring pentacyclic triterpenoid and has been shown to exhibit a variety of biological activities including inhibition of human immunodeficiency virus (HIV), antibacterial, antimalarial, antiinflammatory, anthelmintic, antioxidant and anti-angiogenic properties.
4.1.3. Lenalidomide

Lenalidomide (Fig. 4.1.3.1) is a 3-(4-amino-1-oxo 1, 3-dihydro-2H-isouindol-2-yl) piperidine-2,6-dione, which has recently been approved by the Food and Drug Administration (FDA) for the treatment of a subset of patients with multiple myeloma (MM), a hematological cancer, and myelodysplastic syndromes (MDS), a group of diseases characterized in most patients by refractory peripheral blood cytopenias and hypercellular bone marrow. Lenalidomide is an analogue of the established drug thalidomide, but having a better safety profile than thalidomide.

![Structure of lenalidomide](image)

Fig. 4.1.3.1. Structure of lenalidomide

4.1.3.1. Pharmacokinetics

4.1.3.1.1. Absorption

Rapidly absorbed following oral administration, with $C_{\text{max}}$ occurring 0.625 to 1.5 h postdose reduction of 36% in $C_{\text{max}}$ after administration of food. The pharmacokinetic disposition is linear; $C_{\text{max}}$ and AUC increase proportionately with dose. In multiple myeloma patients, $C_{\text{max}}$ occurred 0.5 to 4 h after administration.

4.1.3.1.2. Distribution

Plasma protein binding is approximately 30%.

4.1.3.1.3. Metabolism

Has not been studied

4.1.3.1.4. Elimination

Approximately 67% is excreted unchanged in the urine and exceeds glomerular filtration rate, indicating elimination is partially or entirely active. The half-life is about 3 h$^{117}$. 
4.1.3.2. Marketed formulation

4.1.3.2.1. Trade name

Revlimid- Capsules 5 mg/ 10 mg/ 15 mg/ 25 mg.

4.1.3.3. Storage/Stability

Store capsules at 59° to 86°F.

4.1.3.4. Pharmacology

It possesses antineoplastic, immunomodulatory and anti-angiogenic properties. Inhibits the secretion of proinflammatory cytokines and increases the secretion of anti-inflammatory cytokines\(^\text{118}\).

4.1.3.5. Mechanism of action of Lenalidomide
4.2. Polymer Profile

4.2.1. Chitosan

Chitosan, (Fig. 4.2.1.1) a natural polysaccharide, comprises of copolymers of glucosamine and N-acetylglucosamine. It is derived by the partial deacetylation of chitin from crustacean shell. The principal sources of chitin are crustacea, insect and fungi. The term chitosan is used to describe a series of chitosan polymers with different molecular weights (50 kDa-2000 kDa), viscosity (1% chitosan in 1% acetic acid < 200 mPas) and degree of acetylation (40-98%).

![Structure of chitosan](image)

**Fig. 4.2.1.1. Structure of chitosan**

**Physicochemical properties**

It is a linear polyamine with a number of amino groups that are readily available for chemical reaction and salt formation. Important characteristics of chitosan are molecular weight, viscosity, degree of deacetylation, crystallinity index, number of monomer units, water retention value, pKa and energy of hydration. It is insoluble at neutral and alkaline pH but soluble in acids and form salts with inorganic and organic acids. The particle size of chitosan is <30mm, density 1.35-1.40 g/cc and pH 6.5-7.5. It is a cationic polyamine with high charge density at pH<6.5, adheres to negatively charge surfaces, forms gels with polyanions having reactive hydroxyl/amino groups.

4.2.1.1. Biological properties

It is nontoxic, biocompatible and biodegradable polymer.
4.2.1. 2. Pharmacological properties

It has hypocholesterolemic action, wound healing properties, antacid and antiulcer activity.

4.2.1. 3. Pharmaceutical applications

Chitosan had excellent properties as an excipient for direct compression of tablets where the addition of 50% chitosan resulted in rapid disintegration. It has been extensively examined in the pharmaceutical industry for its potential in the development of controlled release drug delivery systems. This is due to unique polymeric cationic character and its gel forming properties. Miyazaki et al. 1988 observed the sustaining effect of chitosan on the release of indomethacin from granules. In cancer chemotherapy, chitosan gel microspheres were used for the delivery of anticancer agents to the tumour target cells in sufficient amounts for a desired period of time without any side effect. Chitosan gel used as vehicles for the sustained release of the poorly soluble drugs such as indomethacin and papaverine hydrochlorides. In spite of its well known film forming property, only a few studies have been performed on the usefulness of chitosan membranes as transdermal devices. Microspheres are considered as good potential delivery system to provide a constant therapeutic level of drug and avoid the frequent administration of dosages form. It has been proposed that positive charge on the surface of chitosan give rise to a strong electrostatic interaction with mucus or negatively charged mucosal surface helps in bioadhesion. Chitosan has recently been reported as an absorption enhancer for hydrophilic drugs across the intestinal and nasal mucosa. Interest has been shown in the application of chitosan to deliver peptides or other drugs directly to the colon. Tozaki et al. 1997 investigated the potential of chitosan for colon specific delivery of insulin. The dissolution of poorly soluble drugs is an important factor for drug absorption. It has been found that grinding of chitosan with poorly soluble drugs, such as griseofulvin and prednisolone, enhances their dissolution properties.
4.2.2. Sodium alginate

Sodium alginate (Fig. 4.2.2.1) is a sodium salt of alginic acid with empirical formula NaC_6H_7O_6. Sodium alginate is a gum, extracted from the cell wall of brown algae by the use of dilute alkali. It is a polyuronic acid composed of β-D-mannuronic acid residues linked so that the carboxyl group of each unit is free while the aldehyde group is shielded by a glycosidic linkage. It contains not less than 90.8% and not more than 106.0% of sodium alginate.

![Fig. 4.2.2.1. Structure of sodium alginate](image)

4.2.2.1. Chemical composition

Sodium alginate is a polymer (long molecules made by attaching one after the other a large number from one or several small molecules) made up of two carbohydrates: mannose (M) and glucose (G) along with sodium ions. When calcium ions are added, the polymers wrap around them to form a gel. The way in which these M and G units are arranged in the chain and the overall ratio, M/G, of the two units in a chain can vary from one species of seaweed to another. Generally alginates with a higher content of G will give a stronger gel; such alginates are said to have a low M/G ratio. *Macrocystis* can give a medium-viscosity alginate. *Sargassum* usually gives a low viscosity product. *Laminaria digitata* gives a soft to medium strength gel, while *Laminaria hyperborea* and *Durvillaea* give strong gels. These are some of the reasons why alginate producers like to have a variety of seaweed sources, to match the alginate to the needs of particular applications \([120]\).
4.2.2.2. Physicochemical properties

It occurs as white to yellowish brown filamentous, grainy, granular or powdered forms. Dissolves slowly in water, forming a viscous solution; insoluble in ethanol and ether.

4.2.2.3. Storage

Maximal temperature for storage is 25°C and air moisture < 60%.

4.2.2.4. Pharmaceutical uses

The uses of alginates are based on three main properties. The first is their ability, when dissolved in water, to thicken the resulting solution (more technically described as their ability to increase the viscosity of aqueous solutions). The second is their ability to form gels; gels form when a calcium salt is added to a solution of sodium alginate in water. The gel forms by chemical reaction, the calcium displaces the sodium from the alginate, holds the long alginate molecules together and converts to gel. No heat is required for gel formation and do not melt when heated. The third property of alginates is the ability to form films of sodium or calcium alginate and fibres of calcium alginates. Sodium alginate is a good chelator for pulling radioactive toxins from the body, such as iodine-131 and strontium-90, which have taken the place of their non-radioactive counterparts. It is also used in immobilizing enzymes by inclusion to obtain important products like alcohols, organic acids, etc.

As a flavorless gum, it is used by the foods industry to increase viscosity and as an emulsifier. It is used in indigestion tablets and in preparation of dental impressions. It is also used in combination with chitosan for the formation of novel drug delivery system like microbeads, microspheres, nanosphers etc.
4.2.3. Bovine serum albumin

Bovine serum albumin (Fig. 4.2.3.1) (also known as BSA or "Fraction V") is a serum albumin protein derived from cows. It is often used as a protein concentration standard. The nickname "Fraction V" refers to albumin being the fifth fraction of the original Edwin Cohn purification methodology that made use of differential solubility characteristics of plasma proteins. By manipulating solvent concentrations, pH, salt levels, and temperature, Cohn was able to pull out successive "fractions" of blood plasma. The process was first commercialized with human albumin for medical use and later adopted for production of BSA.

![Structure of bovine serum albumin](image)

**Fig. 4.2.3.1. Structure of bovine serum albumin**

4.2.3.1. Physicochemical properties

- Number of amino acid residues: 585
- Molecular weight: 66,463 Da (= 66.5 kDa)
- Isoelectric point in water at 25 °C: 4.7
- Extinction coefficient of 43,824 M⁻¹cm⁻¹ at 279 nm
- Dimensions: 140 X 40 X 40 Å³ (prolate ellipsoid where a = b < c)

Bovine serum albumin (BSA) is a large globular protein with a good essential amino acid profile. It has been well characterized and the physical properties of this protein are well known by Peters, 1975.

BSA binds free fatty acids, other lipids and flavor compounds, which can alter the heat denaturation of the protein. Isolated BSA has been reported to be a very
functional protein. It is reported to partially unfold between 40 and 50°C, exposing non-polar residues on the surface and facilitating reversible protein-protein interactions. Phospholipid-protein-calcium complexes are formed at pH levels below the isoelectric point of the BSA.

BSA has numerous biochemical applications including ELISA (Enzyme-Linked Immunosorbert Assay), immunoblots, and immunohistochemistry. It is also used as a nutrient in cell and microbial culture. In restriction digests, BSA is used to stabilize some enzymes during digestion of DNA and to prevent adhesion of the enzyme to reaction tubes, pipet tips, and other vessels. This protein does not affect other enzymes that do not need it for stabilization. BSA is also commonly used to determine the quantity of other proteins, by comparing an unknown quantity of protein to known amounts of BSA. BSA is used because of its stability to increase signal in assays, its lack of effect in many biochemical reactions, and its low cost, since large quantities of it can be readily purified from bovine blood, a byproduct of the cattle industry.

4.2.3.2. Pharmaceutical uses

Bovine serum albumin has been its role in the functional properties of whey protein concentrates, and makes up only about 5% of the protein in whey protein concentrates. Its primary biological function has been associated with its lipid binding properties, but the mechanism of this role has not been clearly elucidated. It may play a role in mediating lipid oxidation, since BSA has been shown in-vitro to protect lipids against phenolic induced oxidation. BSA might “reduce the probability of a person acquiring certain diseases, such as insulin dependent diabetes and auto-immune disease. Of these proteins, only the enzyme-hydrolysed casein and BSA were effective against genotoxic compounds. Bovine serum albumin has been used as a component of cell media to regenerate plants from cultured guard cells and to provide for enhancement of production of plasminogen activator.
4.2.4. Mango gum

4.2.4.1. Source and Family

Mango gum (Fig. 4.2.4.1.1) is brown in colour obtained from the bark of Mangifera indica, family Anacardiaceae.

4.2.4.2. Pharmaceutical uses

It is well known in traditional Indian medicine. Various parts such as bark, leaves, roots and kernel seed fruit have served certain purposes, for instance, as diuretic, astringent, diabetes, asthma, diarrhoea, urethritis, dysentery, scabies and other parasitic skin diseases. The Indian researchers explored the feasibility of pharmaceutical and pre-formulation applications of mango gum. They elucidated the physical, thermal, sorption and functional properties of mango gum. The researchers tried Paracetamol (marketed as popular brand name CROCIN) to formulate the tablets using mango gum as excipient. They reported in-vitro drug release more than 90% at 30 min. Tablets with 5 per cent (w/w) binder concentration showed optimum results than standard binder, thus their conclusion was that mango gum was found to be useful for the preparation of uncoated tablet dosage form123.

Fig. 4.2.4.1.1. Image of crude mango gum
4.2.5. Fenugreek

4.2.5.1. Source

Fenugreek (Fig. 4.2.5.1.1) seeds are yellow in colour obtained from *Trigonella foenum-graecum*, family Leguminosae. Its seeds have a strong aroma and somewhat bitter in taste. Fenugreek is native to Southern Europe, the Mediterranean region and Western Asia. It is cultivated from Western Europe to China for the aromatic seeds and is still grown for fodder in parts of Europe and Northern Africa. The seeds are very hard, and difficult to grind. Fenugreek is one such plant whose seeds and leaves are used not only as food but also as an ingredient in traditional medicines.

![Fig. 4.2.5.1.1. Images of fenugreek seeds](image)

In India, the seeds of fenugreek were used in Ayurveda and Siddha to treat fever, dysentery heart diseases and diabetic while in Unani system, this plant issued as a resolvent, aphrodisiac, diuretic, emmenagogue and tonic. In China, fenugreek seeds swear used as a galactogogue to encourage lactation. The past phytochemical investigations on the seeds reveals the presence of diosgenin, trigonelline, gitogenin, vicenins 1 and 2, vitexin, quercetin, luteolin, kaempferol, sitosterol etc., moreover the endosperm of the seeds is rich in galactomannan\(^{124}\).
4.2.5.2. Chemical composition

<table>
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<th>Value</th>
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</tr>
<tr>
<td>Crude lipid (%)</td>
<td>7.14 (±0.28)</td>
</tr>
<tr>
<td>Crude protein (%)</td>
<td>28.4 (±0.64)</td>
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<tr>
<td>Crude fibre (%)</td>
<td>9.30 (±0.09)</td>
</tr>
<tr>
<td>Ash content (%)</td>
<td>3.28 (±0.09)</td>
</tr>
<tr>
<td>Total carbohydrate</td>
<td>47.4</td>
</tr>
</tbody>
</table>

4.2.5.3. Pharmaceutical uses

4.2.5.3.1. Home Remedy for Balancing Cholesterol

Studies have found that people who took 2 ounces (56g) of fenugreek seeds each day had significantly (around 14 percent) lower cholesterol levels after 24 weeks, and had lowered their risk of heart attack by more than 25 percent. Therefore, a recommended remedy for lowering cholesterol is to take 2 ounces of seeds throughout the day. The seeds can be sprinkled onto prepared food, or they can be consumed with water.

4.2.5.3.1. Treating diabetes and lowering blood sugar levels

Studies have shown that individuals with type 2 diabetes had significantly lower blood sugar levels after eating fenugreek. Therefore, a recommended home remedy for treating Type 2 diabetes is to consume 500 mg of fenugreek twice daily.

4.2.5.3.2. Herbal cure for skin inflammation

Research has shown that fenugreek is an effective topical treatment for skin problems such as abscesses, boils, burns, eczema, and gout. Therefore, a simple skin inflammation remedy is the following:

Take a spoonful of fenugreek and grind it into a powder.

- Mix the ground powder with warm water.
- Take a simple piece of clean cloth and soak it into the mixture.
- Apply the soaked cloth directly onto the affected skin as a poultice.
4.2.5.3.3. Natural cure for heartburn and acid reflux

Fenugreek seeds contain a lot of mucilage, which helps soothe gastrointestinal inflammation by coating the lining of the stomach and intestine. Therefore, for an effective remedy against heartburn or acid reflux, simply sprinkle 1 teaspoon of fenugreek seeds onto your food. Another option is to take one teaspoon of seeds and swallow them with water or juice before any meal.

4.2.5.3.4. Home remedy for fever

The Fenugreek herb has been known to help reduce fever when taken with lemon and honey, since it nourishes the body during an illness. Therefore, to treat a fever, simply consume one to two teaspoons of fenugreek seeds three times a day along with an herbal tea (such as green tea) with a teaspoon of honey and lemon juice. Some health food stores also sell herbal Fenugreek teas, which can be used instead of the green tea.

4.2.5.3.5. Remedy to ease child birth for pregnant women

Fenugreek stimulates uterine contractions and can be helpful to induce childbirth. However, pregnant women should only use this remedy for inducing labor after consulting with their doctor.

4.2.5.3.6. Remedy to aid milk production in lactating women

Fenugreek has been known to increase milk production in lactating women. Research has even shown that milk production can increase by over 500 percent within 24 to 72 hours after consuming this herb. Although it is not known why this happens, researchers speculate that the oil contained in fenugreek seeds plays a role. Therefore, a recommended remedy to increase milk flow is to consume one capsule of fenugreek seed (at least 500mg) three times a day.
4.2.6. Ispaghula

4.2.6.1. Source

Ispaghula seeds (Fig. 4.2.6.1) are brown in colour obtained from Plantago ovata Forsskaol. The seeds of psyllium are used commercially for the production of mucilage. The mucilage obtained from the seed coat by mechanical milling/grinding of the outer layer of the seeds. It is a white fibrous hydrophilic material and forms the clear colorless mucilaginous gel by absorbing water. The gel nature and composition of the polysaccharides extracted from the seeds of the P. ovata has been reported in literature.

4.2.6.2. Chemical composition

Ispaghula seeds contains ~15% of non-polysaccharide material and the remaining 85% appears to consist of a single polysaccharide comprising D-xylose (~62%), L-arabinose (~20%), L-rhamnose (~9%) and D-galactouronic acid (~9%). The sugars present and their approximate proportions were first determined by Laidlaw and Percival. Out of two polysaccharide fractions separated from the husk mucilage; one (eq.wt.700; uronic acid 20%) is soluble in cold water while another (eq.wt.4000; uronic acid 3%) is soluble in hot water. The polysaccharide has a linear back bone of β-D-xylose residues in the pyranose ring form and disaccharide side chains with terminal α-D-galactouronic acid linked to O-2- of α-L-rhamnose. All the three side chains are attached to either O-2 or O-3 of xylose in the polymer back bone.
The backbone has both (1>3) and (1>4) -ß- linkages but their sequence and the distribution of side chains, have not yet been determined\textsuperscript{125}.

4.2.6.3. Dose

Oral daily dose- Adolescents over 12 years of age, adults, elderly: 7 - 11 g in 1 - 3 divided doses. Children from 6 to 12 years of age: half to two-thirds of the adult dose (3 - 8 g) daily.

4.2.6.4. Pharmacokinetic properties

4.2.6.4.1. Absorption

The Isabgol husk hydrates and swells to form mucilage because it is only partially solubilised. Less than 10% of the mucilage gets hydrolyzed in the stomach where mainly free arabinose is well absorbed.

4.2.6.4.2. Progress of action

Ispaghula husk usually acts within 12 to 24 hours after single administration. Sometimes the maximum effect is not reached for 2 or 3 days.

4.2.6.4.3. Elimination

Human intestinal flora in the large intestine degrades the polysaccharides.

4.2.6.5. Pharmaceutical uses

Ispaghula husk is an herbal medicine and used for the treatment of habitual constipation. In conditions in which easy defecation with soft stools is desirable, e.g. in cases of painful defecation after rectal or anal surgery, anal fissures and hemorrhoids. In patients to whom an increased daily fibre intake may be advisable e.g. as an adjuvant in constipation predominant irritable bowel syndrome, as an adjuvant to diet in hypercholesterolemia.

Psyllium has been reported as a medicinally active natural polysaccharide. It has been used for the treatment of constipation, diarrhea, inflammation bowel diseases-ulcerative colitis, obesity in children and adolescents, high cholesterol, diabetes, colorectal cancer and ulcerative colitis etc.
4.2.7. Geletin A

Gelatin (Fig. 4.2.7.1) has good mucoadhesive properties and is well tolerated after ophthalmic administration due to its biocompatibility and biodegradability it is widely utilized in pharmaceutical and medical applications. It is a natural polymer consists of the mixture of peptides and proteins produced by partial hydrolysis of collagen extracted from the skin, boiled crushed bones, connective tissues, organs and some intestines of animals such as domesticated cattle, chicken, horses hooves, and pigs.

![Image of gelatin A](image_url)

**Fig. 4.2.7.1. Image of gelatin A**

4.2.7.1. Physico-chemical properties

Gelatin is a translucent, colorless, brittle (when dry), flavorless solid substance. Commercially gelatin is available in two types; type A and type B. Gelatin type A is the acid processed collagen, whereas gelatin type B is derived from alkaline treated collagen. These processed gelatins have different isoelectric points, 7-9 for type A and 4-5 for type B. An absorbable cross-linked hydrogel of gelatin can be easily prepared by thermal and chemical modification. This treated hydrogel does not dissolve in water rather it swells upon contact with water.
4.2.7.2. Pharmaceutical uses

Gelatin based ocular delivery systems can be optimized by changing the electrical and physical properties of gelatin. For example, an aqueous solution of gelatin acts as a thermoreversible hydrogel. This hydrogel has low mechanical strength and starts to break at 30 °C that result in drug loss. Gelatin chains can be crosslinked chemically to provide stability towards thermal degradation. Available literature described the carbodiimide crosslinked gelatin hydrogel loaded with pilocarpine hydrochloride for the treatment of glaucoma. They observed that the water uptake of hydrogel was reduced by crosslinking, which resulted in slower release of pilocarpine hydrochloride from the gel matrix. In addition, they found that the degree of crosslinking played a major role in both mechanisms. They also prepared the lyophilisates of the gelatin and observed the similar effects of crosslinking. In another study, release of pilocarpine was optimized by embedding the gelatine hydrogel with cetyl ester wax and polyethylene glycol. This strategy had provided zero order release of pilocarpine from the hydrogel due to slower penetration of water inside the matrix. Vandervoort et al prepared gelatin nanoparticles encapsulating pilocarpine HCl and hydrocortisone for topical ophthalmic applications. These investigators examined the effect of various parameters (such as gelatin type and pH) on the preparation of nanoparticles. They concluded that gelatin could be an effective polymeric carrier due to prolonged residence time at the ocular surface. Gelatin was extensively employed for fabrication of ocular devices such as microspheres and microcapsules.

4.2.7.3. Other uses

Certain professional and the atrical lighting equipment use color gels to change the beam color. It is used to hold silver halide crystals in an emulsion in virtually all photographic films and photographic papers. It is used as a carrier, coating or separating agent for other substances; for example, it makes beta-carotene water-soluble thus imparting a yellow colour to any soft drinks containing beta-carotene. Cosmetics may contain a non-gelling variant of gelatin under the name hydrolyzed collagen. Gelatin was first used as an external surface sizing for paper in 1337 and continued as a dominant sizing agent. In modern times it occasionally found in some glossy printing papers, artistic papers, playing cards, and it maintains the wrinkles in crêpe paper.