CHAPTER-2

REVIEW OF LITERATURE

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2.1. Current Allopath treatment of obesity:

As we know there are so many marketed formulations in allopathic system available for the treatment for obesity but us also aware that they are having several uncontrolled side effects. They are having different targets to treat the obesity. There are some class of the drugs mention here which are used.

Sr.No.	Medicines	Side effects
1	Simvastatin	Myalgias and Rhabdomyolysis.
2	cholestyramine	Constipation, nausea, and May increase triglycerides;
3	orlistat	Diarrhea, gas, leakage of oily stools and stomach pain
4	Niacin	Flushing is common; may be reduced with aspirin pre treatment May increase uric acid and glucose levels.
5	clofibrate	Gastrointestinal upset, rash, and abdominal pain are common.

Table 2.1 Drugs used for obesity

2.2 Current Herbal approach for the obesity:

Herbal plants for weight reduction may be effective in the treatment of obesity and associated disorders. Consistent and safe herbal product for weight reduction is a need of developed and developing countries. In our literature survey, herbal plants showed potential effects on weight control. A variety of natural products, including crude extracts and isolated compounds from plants, can induce lipid profile reduction and prevent obesity. Therefore, they have been widely used in treating obesity. The botanical drugs can be developed faster

and cheaper than conventional single-entity pharmaceuticals. Botanicals are safe, natural, and cost effective alternatives to synthetic drugs.

Sr.No.	Formulation	Content
1	Herboslim	MedoharGuggul, Garcinia Methi, Musta, Apamarg kshar, and Pippali
2	Vrikshamla	Garcinia cambogia fruit rind extract
3	Slimonil	Medohar Guggulu 250 mg, Vidang (Embelia Ribes) 50 mg, Vijayasar (Pterocarpus Marsupium Stick) 50 mg, Punarnava (Borhavia Diffusa) 50 mg, Rudrajata (Aristolochia Galanga) 25 mg, Pippalimul (root of piper longum) 25 mg.
4	Weight Loss	Coffee, Garcinia, Green Tea, Black Pepper

Table 2.1Herbal approach for the obesity

2.3. Current target for Drug targets of obesity:

At present situation so many herbal drugs and nutraceutical products available in the market for either as a treatment or management of obesity. These available sources does not having same response for obesity. The main reason behind this is maintain the energy balance in the body and maintain the energy level in both ways input and output. Purpose to select the targets are they importance are distinctive so all follow different mechanism of action. The basic principle behind ant obesity drugs are maintains the energy balance in the body that is symmetry between energy intake and expenditure [(1)]. The main practices follow either effect of these drugs on nervous system or effect of diet on physiological function. All targets by which ant obesity drugs are designated as pancreatic lipase enzyme inhibition, Thermogenesis, Lipid Metabolism and Centrally acting mechanism.

In Pancreatic lipase inhibition: food is absorbed in the stomach and this enzyme converts fats in to free fatty acids and glycerides. Inhibition of this enzyme ultimately leads to reduce the obesity. Drug likes orlistat having same mechanism. Many reported herbs are also having the same mechanism, herbs like Garcinia,

Thermogenesis: By the metabolism of food there is a generation of ATPs that's how it convert the food energy as heat and it lastly reduce the obesity. There are three types of adipose tissue: White, brown and beige adipose tissue. In mechanism, brown adipose tissue plays key role in obesity by convert the food energy as heat. Herbs like Coffee and many phenolic compounds have the same reported effect.

Lipolysis: In lipolysis there is a hydrolysis of triglycerides and that's how reducing the storage fat. Herbs like green tea and ketone (Raspberry, Blue berry) having the same mechanism to act in obesity.

Leptin: Leptin is a hormone. Your body releases that help it keep your normal weight on a long-term basis. Leptin largely acts on your brainstem and hypothalamus to control hunger and energy balance, though you have leptin receptors in other areas of your body. Leptin booster can help to control the obesity. Leptin directly trigger your CNS and satiety peptide. This can control your appetite. And during such condition to compensate the energy requirements body used the storage fats and reduce the obesity. Herbs like green tea, Garcinia and ketone (Raspberry, Blue berry) having the same mechanism to act in obesity.

2.4. Selection of medicinal plants for tablet formulation:

Many medicinal plants are used in the treatment of the obesity. These plants are used directly in crude form or different extract form. This crude powder or extract is than convert in to different suitable dosage form. As we know good source of medicinal plants are available in the nature. Many medicinal plants are having different report towards the obesity. The Herbal formulation can be developed faster and cheaper than conventional formulations. These medicinal plants are safe and cost effective than synthetic drugs. Different plants having different mechanism to treat the obesity based on the presence of the active metabolites like flavonoids, alkaloids, glycosides and phenolics.

Following are the plants reported in the treatment of obesity

	Plant name	**Part(s)**	**Mechanism**
1	*Achyranthes aspera* Linn (Amaranthaceae)	Seed	The plant lowers total cholesterol, total triglyceride, and LDL-cholesterol, and increases HDL cholesterol level.
2	*Acorus calamus* Linn (Araceae)	Rhizome, rootsand leaves	Ethyl acetate extarct of *A. calamus* inhibits α-glucosidaseactivity.

3	*Achyranthes bidentata* Blume (Amaranthaceae)	Root	The drug affects on differentiation of adipocyte anddecrease of phospho-Akt expression.
4	*Actinidia polygama* Max (Actinidiaceae)	Fruits	Serum levels of aspartate decreased in the mice treated with the extract without changes in serum levels of alanine transaminase blood urea nitrogen and creatinine.
5	*Adenophora triphylla* Hara (Campanulaceae)	Root	Anti-obesity effect of *A. triphylla* is mediated by increasing adipocytes adiponectin and activating pathway like AMPK, and PPAR-α, and decreasing adipokines TNF-α, GPDH, and PPAR-α. It also actively expresses low-density lipoprotein [LDL] receptor and cholestorl 7α-hydroxylase (CYA7A1) and inhibits expression of 3 hydroxy-3 methyl glutaryl - CoA (HMG-CoA) reductase.
6	*Aegle marmelos* Linn (Rutaceae)	Leaves	The active chemical constituents of *A. marmelos* for anti- adipogenic activity are halfordinol, ethyl ether aegeline and esculetin were responsible for the decrease in adipocyte accumulation. Active compounds umbelliferone and esculetin depletes lipid content in the adipocytes and by decreasing the hyperlipidemia.
7	*Allium cepa* Linn (Amaryllidaceae)	Peel	The mRNA levels of activating protein (AP2) is down- regulated by *A.cepa* and those of carnitine palmitoyl transferase-1 α (CPT-1α) and fatty acid binding protein 4 (FABP4) are up-regulated. It is also proposed that *A. cepa* increases level of PPAR-γ2 mRNA (mesenteric fats) and IL-6 mRNA levels (perirenal and mesenteric fats).
8	*Allium fistulosum* Linn (Liliaceae)	Root	Significant reduction in body weight and adipose tissue weight as well as adipocyte size. Genes involved in lipogenesis are down-regulated by *A. fistulosum*.
9	*Allium nigrum* Linn (Amaryllidaceae)	Bulb	Extract of *A. nigrum* upregulates AMPK, FOXO1, Sirt1, ATGL, HSL, perilipin, ACO, CPT-1, and UCP1 in the adipose tissues, whereas it downregulates CD36.
10	*Allium sativum* Linn (Amaryllidaceae)	Stem, Bulb and Roots	It increases antioxidant enzymes and suppresses glutathione depletion and lipid peroxidation in hepatic tissue. Oil isolated from *A. sativum* down regulates sterol regulatory element binding protein-1c, acetyl- coA carboxylase, fatty acid synthase, and 3-hydroxy-3- methylglutaryl-coenzyme A reductase.
11	*Alpinia galanga* Linn (Zingiberaceae)	Rhizome	Galangin, the principal compontent of *A. galangal* decreases serum lipids, liver weight, lipid peroxidation and accumulation of hepatic TGs.
12	*Alpinia officinarum* Hance (Zingiberaceae)	Root	The drug controls and improves lipid profile in animals by lowering serum Total-C, TG, and LDL-C concentrations, leptin content.

13	*Angelica gigas* Nakai (Apiaceae)	Roots	Decursin, the active constituent of *A.gigas* improves glucose tolerance. Decursin along with the HFD significantly reduces secretion adipocytokines such as leptin, resistin, IL-6 and MCP-1.
14	*Argyreia nervosa* Bojer (Convolvulaceae)	Root	Serum contents of leptin, total cholestrol, LDL, and triglycerides are reduced by *A. speciosa*.
15	*Artemisia iwayomogi* (Compositae)	Whole Plant	It downregulates adipogenic transcription factors PPARγ2 and C/EBPα and their target genes CD36, aP2, and FAS. The extract decreases gene expression of proinflammatory cytokines including TNFα, MCP1, IL-6, IFNα, and INFβ in epididymal adipose tissue and reduces plasma levels of TNFα and MCP1.
16	*Atractylodes lancea* (Thunb.) DC (Compositae)	Rhizome	It inhibits human pancreatic lipase. A new polyacetylene, *syn*-(5*E*,11*E*)-3-acetoxy-4-O-(3-methylbutanoyl)-1,5,11- tridecatriene-7,9-diyne-3,4-diol has been isolated and identified and exhibits lipase inhibitory activity.
17	*Aster pseudoglehni Lim, Hyun & Shin (Asteraceae)*	Leaves	It suppresses expression of adipogenesis-related genes including PPARγ, C/EBPα, and SREBP1c.
18	*Bauhinia variegata* Linn (Leguminosae)	Stem and root barks	Extract of *E. variegata* increases brain serotonin level and high-density lipoprotein with a concomitant decrease in total cholesterol, triglycerides and low-density lipo protein.
19	*Bergenia crassifolia* (L.) Fritsch (Saxifragaceae)	Leaves	Galloylbergenin derivatives 3,11-Di-O-galloylbergenin and 4,11-di-O-galloylbergenin are found to be present in *B. crassifolia* moderates anti-lipid accumulation activities.
20	*Boehmeria nivea* (L.) Gaudich (Urticaceae)	Leaf	The extracts reduces adipose tissue weight serum alkaline aminotransferase and lactate dehydrogenase activities. Serum triglyceride, total cholesterol, LDL-cholesterol level, atherogenic index and cardiac risk factors are decreased in animals fed with leaf powder and serum HDL - cholestrol levels are increased.
21	*Boerhaavia diffusa* L. (Nyctaginaceae)	Root	The phytoconstituents compounds sitosterol found in this plant which is structurally similar to cholesterol has been suggested to reduce cholesterol by lowering the level of LDL-cholesterol and cholesterol level decreased significantly in plasma without any side effects.
22	*Bombax ceiba* L. (Malvaceae)	Stem bark	The extract and active constituent gemfibrozil reverses the effects of HFD treatment on serum parameters. This activity may be due to the inactivation of acetyl-coA carboxylase, as a result of AMPK activation that mediates thermogenesis and FAS inhibition.

23	*Anredera cordifolia* (Ten.) Steenis (Basellaceae)	Leaves	The extract suppresses lipid accumulation and down- regulates PPARγ, CCAAT/enhancer binding protein α, SREBP, and their target genes. It also increases phosphorylation of AMPK.
24	*Brassica rapa* L. (Brassicaceae)	Root	Lipolysis-related genes including β_3-adrenergic receptor, hormone-sensitive lipase, adipose triglyceride lipase, and uncoupling protein are induced in white adipocytes of animals treated with extract of *B. campestris*.
25	*Buddleja officinalis* Maxim (Scrophulariaceae)	Whole Plant	The extract reduces body weight gain induced throughadipocyte differentiation.
26	*Bursera grandiflora* (Schltdl.) Engl (Burseraceae)	Roots	*B. grandiflora* exerts anti-obesity activity by decreasing inthe plasma-triglyceride levels.
27	*Calanus finmarchicus* (Calanidae)	Wax	*C. finmarchicus* reduces macrophage infiltration and downregulates expression of proinflammatory genes including tumor necrosis factor-α, interleukin–6, and monocyte chemoattractant protein–1, whereas up- regulates adiponectin expression.
28	*Camellia japonica* L. (Theaceae)	Leaves	*C. japonica* control insulin which is a modulator of lipid synthesis via sterol regulatory element binding protein- 1c (SREBP-1c), decreased levels of insulin affects hepatictriglyceride synthesis.
29	*Camellia oleifera Abel (Theaceae)*	Fruit hull	*Serum levels of total cholesterol and triacylglycerols are decreased but high-density lipoprotein cholesterol increased.Activity of fatty acid in animal liver is loweredby.*
30	*Camellia sinensis* (L.) Kuntze (Theaceae)	Leaves, twigsand stems, flower buds	*C. sinesis* attenuates the gene expression of (SREBP-1c), fatty acid synthase and CCAAT/enhancer binding protein α. Extract found to reduce sICAM-1 release followed by nonpharmacological HGTE supplementation in db/db mice causing no adiponectin-inducing or antiadipogenic effects, reduced sICAM-1 release. Chakasaponin II from flower bud, suppresses mRNA levels of neuropeptide Y (NPY). The mRNA levels of adipogenic genes such as PPAR-γ, C/EBP-α, SREBP-1c, adipocyte fatty acid-binding protein, lipoprotein lipase and fatty acid synthase are decreased in *C. Sinensis* treated animals.
31	*Cheilanthes albomarginata* C.B. Clarke (Pteridaceae)	Rhizome	Extract of *C. albomarginata* lowers plasma triglyceride activity as well as reduces weight of adipose tissue.
32	*Chenopodium quinoa* Willd (Amaranthaceae)	Seeds	*C. quinoa* extract attenuate mRNA levels of several inflammation markers including monocyte chemotactic protein-1, CD68 and insulin resistance osteopontin, plasminogen activator inhibitor-1 and it also reverses the effects of HF-induced downregulation of the

			uncoupling protein(s) mRNA levels in muscle.
33	*Cirsium brevicaule* A. Gray (Compositae)	Leaves	*C. brevicaule* inhibits fatty acid synthase and suppress the differentiation and lipid accumulation and affecting transcription factors such as SREBP-1c, C/EBPα, and PPARγ known to control the fatty acid synthase expression.
34	*Citrus reticulata* Blanco (Rutaceae)	Peel	mRNA expression levels of lipogenesis rrelated genes such as SREBP1c, FAS and ACC1 in the liver are lowered and the size of adipocytes are reduced.
35	*Citrus sunki* (Hayata) Yu.Tanaka (Rutaceae)	Peel	Phosphorylation levels of AMPK and acetyl-CoA carboxylase are decreased.
36	*Clerodendrum phlomidis* L. f. (Lamiaceae)	Roots	It nhibits pancreatic lipase activity. The extract contains β-sitosterol.
37	*Coccinia grandis* (L.) Voigt (Cucurbitaceae)	Fruit	Reduces body weight, food intake, organ and fat pads weight and serum GLU, CHO, TRG, LDL and VLDL cholesterol levels and increases HDL levels.
38	*Codonopsis lanceolata* (Siebold & Zucc.) Benth. & Hook.f. ex Trautv (Campanulaceae)	Roots	Reduces weight of adipose pads and the serum levels of triglycerides, total cholesterol, and low density lipoprotein cholesterol.
39	*Coffea arabica* L. (Rubiaceae)	Seed	*C. arabica* diet supplementation can impair glucose tolerance, hypertension, cardiovascular remodeling, and nonalcoholic fatty liver disease.
40	*Coleus forskohlii* (Willd.) Briq. (Lamiaceae).	Root	*C. forskohlii* act as anti-obesisity drug by inhibiting dyslipidemia.
41	*Corchorus olitorius* L. (Malvaceae)	Leaves	Liver tissue gene expression of gp91phox (NOX2) involved in oxidative stress is down-regulated by *C. olitorius* and genes related to the activation of β-oxidation like PPARα and CPT1A are up-regulated by the plant.
42	*Cordia ecalyculata* Vell (Boraginaceae)	Whole plant	Anti-obesity activity of the *C. ecalyculata* is medicated by anorectic central action, facilitating binding to adenosine receptors, thereby promoting an extension of adrenalin.
43	*Cornus officinalis* Siebold & Zucc. (Cornaceae)	Rhizome	Platycodin D is the major component effective to activate AMPK-α. The extract reduces serum levels of aspartate transaminase and alanine transaminase.
44	*Cucumis melo* L. (Cucurbitaceae)	Fruit peel	*C. melo* reduces gain in body weight, serum lipid profile like total cholesterol, triglyceride, LDL-C level, atherogenic index and increases serum HDL-C levels.
45	*Cyamopsis tetragonoloba* (L.) Taub (Leguminosae)	Beans	It decreases adipose triglyceride accompanied by enhancing activity of hormone-sensitive lipase-facilitating mobilization of depot fat.

46	*Dimocarpus longans* Leenh (Sapindaceae)	Flower	By combined effect of decreased exogenous lipid absorption, normalization of hepatic PPAR-γ gene expression, suppression of pancreatic activity and SREBP- 1c and FAS gene expression, and higher fecal triglyceride output.
47	*Dioscoreae tokoronis* Linn (Dioscoreaceae)	Root	It decreases triglyceride, total plasma cholesterol, and low-density lipoprotein-cholesterol. It suppresses the expression of SREBP-1 as well as that of fatty acid synthase in adipose and liver tissues.
48	*Eucommia ulmoides* Oliv (Eucommiaceae)	Leaves, Bark	Asperuloside increases adenosine 5′-triphosphate production in WAT and increases use of ketone bodies/ glucose in skeletal muscle.
49	*Fraxinus excelsior* L.(Oleaceae)	Seed	Secoiridoids present enhances fat metabolism through β-oxidation, inhibit adipocyte differentiation during animal growth and limit fat accumulation.
50	*Garcinia cowa* Roxb. ex Choisy (Clusiaceae)	Fruit, commercially available tablet	Inhibits the enzyme ATP-dependent citrate lyase, which catalyzes the cleavage of citrate to oxaloacetate and acetyl-CoA.Serum apo A1 levels are increased by the plant and the serum total cholesterol levels.
51	*Geranium thunbergii* Siebold ex Lindl. & Paxton (Geraniaceae)	Leaf	The extract ameliorates high-fat diet-induced obesity by altering the adipokine levels and downregulates expression of transcription factors and lipogenic enzymes involved in lipid metabolism.
52	*Glycine max* (L.)Merr. (Leguminosae)	Bean	Reductions glucose-6-phosphate dehydrogenase, malic enzyme, fatty acid synthetase, as well as acetyl-CoA carboxylase. The extract decreases appetite and HF diet-induced body weight gain through leptin-like STAT3 phosphorylation and AMPK activation.
53	*Gymnema sylvestre* (Retz.) R.Br. ex Sm (Apocynaceae)	Leaves	Inhibits serum lipids, leptin, insulin, glucose, apolipoprotein B and LDH levels while it increases the HDL-cholesterol, apolipoprotein A1 and antioxidant enzymes levels.
54	*Hibiscus cannabinus* L.(Malvaceae)	Leaves	It decreases serum cholesterol, triglycerides, LDL-C, SGOT and SGPT activities.
55	*Hibiscus sabdariffa* L.(Malvaceae)	Leaf	Promotes LXRα/ABCA1 pathway, stimulating cholesterol removal from macrophages, delaying atherosclerosis. Also, the extract treatment attenuated liver steatosis, downregulated SREBP-1c and PPAR-γ, blocked the increase of IL-1, TNF-α mRNA and lipoperoxidation and increased catalase mRNA.
56	*Holoptelea integrifolia* (Roxb.) Planch. (Ulmaceae)	Bark	HMG-CoA reductase activity is reduced and cholesterol biosynthesis and increase in lecithin, cholesterolacyltransferase activity.
57	*Humulus lupulus* L. (Cannabaceae)	Female inflorescence	Hepatic fatty acid synthesis is reduced through the reduction of hepatic SREBP1c mRNA expression in the rats fed a high-fat diet.

58	*Hunteria umbellata* (K.Schum.) Hallier f.(Apocynaceae)	Seed	The extract reduces weight gain pattern and causes dose related reductions in the serum lipids, Coronary artery risk index. Also, pre-treatment significantly improves triton-induced hepatic histological lesions.
59	*Hypericum philonotis* Schltdl. & Cham. (Hypericaceae)	Leaves	Decreases body weight and serum glucose levels. It also decreases total cholesterol, triglycerides and high-density lipoprotein-cholesterol without changing low-density lipoprotein-cholesterol, AI, AST and ALT level.
60	*Hypericum silenoides* Juss. (Hypericaceae)	Leaves	Body weight and serum glucose levels of the rats decreased. The drug also has effect on total cholesterol, triglycerides and high-density lipoprotein-cholesterol.
61	*Ilex paraguariensis* A.St.-Hil. (Aquifoliaceae)	Leaves and unripe fruits	Down-regulates expression of Creb-1 and C/EBPa, and up-regulates expression of Dlk1, Gata2, Gata3, Klf2, Lrp5, Pparc$_2$, Sfrp1, Tcf7l2, Wnt10b, and Wnt3a. The mRNA levels of PPAR-γ2 were downregulated.
62	*Ipomoea batatas* (L.) Lam (Convolvulaceae)	Fruit	Expression of SREBP-l, Acyl-CoA Synthase, Glycerol-3- Phosphate Acyltransferase, HMG-CoA Reductase and Fatty Acid Synthase in liver tissue in mice is altered.
63	*Saccharina japonica* (Phaeophyceae)	Whole Plant	Expression of the fat intake-related gene ACC2 and lipogenesis-related genes are reduced. It increases phosphorylation of AMPK and its direct downstream protein, acetyl coenzyme A carboxylase.

From the above list of the herbs following herbs are selected for the formulation

- ✓ *Garcenia indica (Fruit)*
- ✓ *Murraya koenigii (Leaves)*
- ✓ *Commiphora mukul* (Gum)
- ✓ *Achyranthes aspera* (Seed)

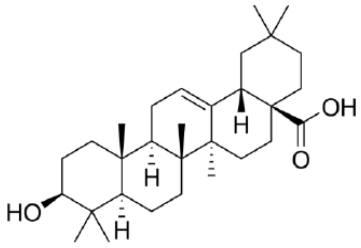
2.5. Achyranthes aspera (Seed)

It consists of dried seeds of *Achyranthes aspera (L.)* belonging to family Amaranthaceae. It is normally known as “Aghedo” and “Prickly chaff plant” in English due its look.

Figure2. 1*Achyranthus Aspera* Seed

2.5.1 Chemical constituents of *Achyranthus Aspera*

Chemical investigations of the seeds of Achyranthes aspera by V. Hariharan & S. angaswami (1970) and M. Ali (1993) reported the isolation & identification of Saponins A and B. Saponin A was identified as D-Glucuronic Acid and saponins B was identified as β-galactopyranosyl ester of D-Glucuronic Acid. Along with these constituents certain other constituents were also isolated like oleanolic acid, amino acids and hentriacontane. The seeds also contain chemical constituents like 10-tricosanone, 10-octacosanone & 4-tritriacontanone (44, 45, 46).



Oleanolic acid

2.5.2 Pharmacological Application:

phytochemical constituents which are isolated from the plant they are having possesses actions like antiperiodic, diuretic, purgative, laxative, anti-asthmatic, hepatoprotective, anti-allergic and various other vital medicinal properties. The plant is used in Ayurveda as emenagogue, antiarthritic, antifertility, laxative, ecbolic, anti-helminthic, aphrodisiac, antiviral, anti-plasmodic, and antihypertensive, anti coagulant, diuretic and anti-tumour. It is also useful to treat cough, renal dropsy, fistula, scrofula, skin rash, nasal, infection, chronic

malaria, impotence, fever, asthma, piles and snake bites. This plant is astringent, digestive, diuretic, laxative, purgative and stomachic. The juice of this plant is used in the treatment of boils, diarrhoea, dysentery, haemorrhoids, rheumatic pains, itches and skin eruption [47].

2.6. Murraya Koenigii(L) Leaves:

Leaves of *Murraya Koenigii(L) Spreng* (Rutaceae) is commonly known as curry leaves or Mittha neem which is widely being used as flavoring agent in curries, and other foodstuffs since ancient times. The Rutaceae family represents more than 150 genera and 1600 species. Among 14 global species belongs to the genus of Murraya, only *Murraya Koenigii Spreng* and *Murraya Paniculata (Linn)* jack is available in India [43].

Figure 2Murraya Koenigii(L) Leaves

2.6.1 Chemical Constituents:

The matured curry leaves consist 63.2% of moisture, protein which is of about 1.15% of nitrogen, carbohydrate 14.6% which is of total sugars and total ash 13.06%. The bioactive components in curry leaves are oxalic acid, resin, carbazole alkaloids and the major bioactive compounds such as the koenigin, bicyclomahanimbicine, cyclomahanimbine, murrayastine, coumarine, koenidine and pypayafolinecarbazole has signaficant pharmacological activities and the major portion of volatile oil consist of bicyclomahanimbicine, mahanimbicine.

2.6.2 Pharmacological Applications:

Murraya Koenigii(Curry leaf tree) has been used in several ancient systems of medicine including Siddha and Unani as a multipotential medicinal plant. The whole plant is a rich source of carbazole alkaloids and these alkaloids have been reported for their various pharmacological activities such as antiemetic, antidiarrhoeal, blood purifier and febrifuge. It is also been reported as antidiabetic, antioxidant, antihypertensive, antibacterial, cytotoxic and also in the treatment of various respiratory tract disorders. The whole plant is used as a tonic and stomachic. The leaves are also been used externally to treat burns, bruises and skin eruption. It is also been used in preventing premature greying of hair [(43)].

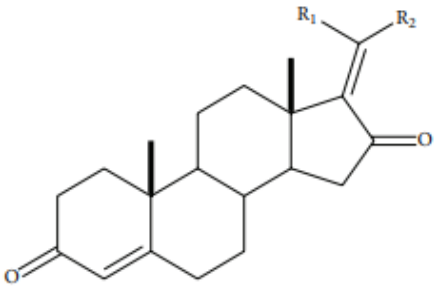
2.7. Guggul:

Guggal is a gum resin obtained by incision of the bark of *Commiphora mukul* belonging to family Burseraceae. uggal occurs as viscid, brown tears; or in fragment pieces, mixed with stem, piece of bark; golden yellow to brown in colour. With water it forms a milk emulsion. It has a balsamic odour and taste is bitter, aromatic.

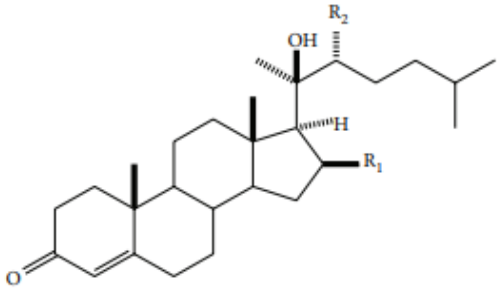
Figure 2.3Commiphora mukul

2.7.1 Chemical Constituents:

Guggal contains gum (32%), essential oil (1.45%), sterols (guggulsterols I to VI, β-sitosterol, cholesterol, Z- and E-guggulsterone), sugars (sucrose, fructose), amino acids, α-camphorene, cembrene, allylcembrol, flavonoids (quercetin and its glycosides), ellagic acid, myricyl alcohol, aliphatic tetrols, etc. Gum resin contains about 1 -1.5% w/w guggulosterone Z and E as per I.P.2010.



	R_1	R_2
(23) *E*-Guggulsterone	CH_3	H
(24) *Z*-Guggulsterone	H	CH_3



	R_1	R_2
(25) Guggulsterol-I	OH	OH
(26) Guggulsterol-III	OH	H
(27) 20*R*,22*R*-Dihydroxycholest-4-en-3-one	H	OH

2.7.2 Pharmacological Application:

Hypolipidemic Activity: The lipid lowering effect of guggulu with special reference to atherosclerosis and obesity (medoraga) was first reported in a doctorate thesis submitted to the Banaras Hindu University (BHU) in January 1966. Earlier to this work, guggulu was well known as an Ayurvedic drug for the treatment of various types of arthritis. This work was inspired by a rather obscure shloka in Sanskrit in the well-known Ayurvedic treatise Sushruta Samhita. The shloka deals in an extraordinarily lucid and scientific manner, with the etiology, pathogenesis, and treatment of obesity and associated lipid disorders and their complications. The hypolipidemic activity was shown in animals as well as in patients of obesity and hypercholesterolemia [(48)].

2.8. *Garcinia indica* fruit:

Garcinia indica is an underexploited fruit species, which is a rich source of anthocyanin. It is commonly known in India as Kokum, brindon or bhirand, or anslil, murgal, punarpulli. It belongs to the family of Guttiferae. Garcinia species are also spread throughout the tropical Asian and African countries and have incredible potential as a colorant, spice with medicinal value. It is originate in India in tropical humid evergreen rain forests of Western Ghats of south India as well as in northeast states of India. More than 200 listed species of Garcinia are available worldwide and out of these 30 species are reported to be available in India [(49)].

Figure 2.4 Garcinia Indica Fruit

2.8.1 Chemical Constituents:

The rind contains moisture (80.0 g/100 g), protein (1%), tannin (1.7%), pectin (0.9%), Total sugars (4.1%) and fat (1.4%). Garcinia leaves are stated to contain 75% moisture, 2.3 g of protein, 0.5 g of fat, 1.24 g fiber, 17.2 g of carbohydrates, 15.14 mg of iron, 250 mg of calcium, 10 mg of ascorbic acid and 18.10 mg of oxalic acid. The seed is very rich in stearic, oleic and stearic triglycerides. The plant also contains hydroxycitric acid lactone and citric, but in minor quantities. Hydroxycitric acid [(-)-HCA] is the chief acid of fruit rinds of Garcinia cambogia (-)-HCA was shown to be a potent inhibitor of ATP citrate lyase. The inhibition of this reaction limits the availability of acetyl-CoA units required for fatty acid synthesis and lipogenesis during a lipogenic diet, that is, a diet high in carbohydrates is added glycogen load in the liver stimulates a longer lasting neuro- signal from the liver to the brain, representing satiety thus helping to suppress appetite longer. (-)-HCA as weight-controlling agent [(49)].

2.8.2 Pharmacological Application:

Garcinia indica (commonly known as kokum), is a tropical evergreen tree distributed in many regions of India. It has been used in culinary and industrial applications for a variety of purposes, including acidulant in curries, pickles, health drinks, wine, and butter. In particular, G. indica has been used in traditional medicine to treat inflammation, dermatitis, and diarrhea, and to promote digestion. Rendering to several studies, various phytochemicals such as garcinol, hydroxycitric acid (HCA), cyanidin-3-sambubioside, and cyanidin-3-glucoside were isolated from G. indica, and their pharmacological activities were available. This review represent recent updates on the various pharmacological activities of G. indica. These studies reported that G. indica has antioxidant, anti-obesity, anti-arthritic, anti-inflammatory, antibacterial, hepatoprotective, cardioprotective, antidepressant and anxiolytic effects both in vitro and in vivo. These findings, together with previously available reports of

pharmacological activity of various components isolated from G. indica, suggest its potential as a likely therapeutic agent to prevent various diseases [50].

2.9. Herbal Tablet formulation:

Tablets are solid dosage forms containing medicinal agents, with or without any diluents. Compressed tablets are solid dosage forms prepared by compaction of a formulation containing a drug and certain excipients selected to aid in processing and to improve product properties. In Ayurveda many Medicinal Plants used as Anti-obesity agents but they are providing it as in the form of Powders. Most of the herbs from the natural source are moisture sensitive, volatile, and hygroscopic so, the powder shows the moisture sensitivity and stability issues. To overcome this common problem we thought of the herbal tablet using the suitable pharmaceutical excipients. This will help to increase the rate of acceptance and uniformity of dose and stability of the herbal actives. Following are some of the methods which are used for the tablet formulation [51].

2.9.1 Methodology for tablet formulation:

Wet Granulation:

Wet granulation is the process in which a liquid is added to a powder with agitation to produce agglomeration or granules. Wet granules are prepared using oscillating granulators, high-speed mixers, or even fluidized-bed granulators. The wet granules are properly dried and mixed with other essential excipients and finally pressed in a tablet press. This is the oldest and most conventional method of making tablets. It is also the method of choice when large-dose drugs are to be compressed.

Dry Granulation:

Dry granulation involves compression the components of a tablet formulation by means of a tablet press and then milling the compact to obtain the granules. Compaction for the dry granulation process is generally achieved either by slugging or roller compaction. No water or heat is needed for this granulation process. In the slugging process, large tablets are compressed in a heavy-duty tablet press. These tablets are then broken into granules in a conventional mill. In the case of a roller compacter, the powders are pressed in a roller mill,

and the thin sheet of compacted materials is further broken into granules with a conventional mill than it is used for tablet compression.

Direct Compression:

The direct compression process involves the compression of mixed powder components into tablets without an intermediate granulating step. Recently, there has been a great deal of research to develop diluents for direct compression. Some available direct compression diluents include lactose, spray-dried lactose microcrystalline cellulose, calcium sulfate, dibasic calcium phosphate, and starch 1500

2.9.2 Excipients used for tablet:

The excipients used in tablet compression are as follows:

Binder	Usual Concentration (% w/v)
Corn starch USP	5%–10% aqueous paste
Starch 1500	5%–10% aqueous paste
Gelatin	2%–10% aqueous solution
Acacia	5%–20% aqueous solution
PVP	5%–20% aqueous, alcoholic or hydroalcoholic
Methyl cellulose	2%–10% aqueous solution
Sodium carboxymethyl-cellulose	2%–10% aqueous solution

Disintegrants:

Disintegrants	Concentration (% w/w) in Granulation
Starch USP	5–20
Starch 1500	5–15
Microcrystalline cellulose (Avicel)	5–15
Alginic acid	5–15
Guar gum	2–8
Methylcellulose, sodium carboxymethylcellulose	5–10

Super Disintegrants like AC-Di-sol (Na-CMC), Sodium Starch Glycocollate, Cross carmellose sodium Crosspovidone

Lubricants: Talc Magnesium stearate

Dry binder: Cellulose, Methyl cellulose, Polyvinyl pyrrolidone, Polyethylene glycol

SYLOID (silica) is unique combination of adsorption capacity, particle size and surface morphology allows it to provide several functions simultaneously in formulations for: • Pharmaceutical and OTC Drugs • Multi-vitamins/Minerals Preparations

• Dietary and Herbal Supplements

2.9.3 Evaluation Parameters of Tablets

Physical Parameter Like: Appearance, Thickness
Hardness
Disintegration
Weight Uniformity

2.10. Development of methods for analysis of markers present in herbal extracts

2.11.1 Analytical method development

Analytical method development and validation can be unstated as the procedure of showing that analytical measures are satisfactory for the purpose of assessing drugs, and particularly the active pharmaceutical ingredient (API).

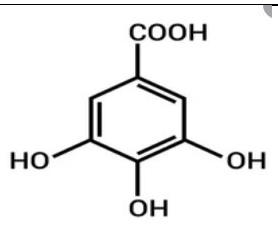
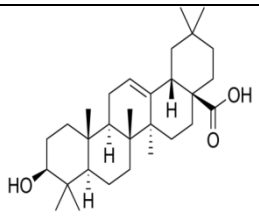
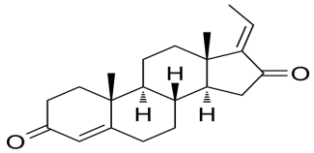
Method development is a continuous processes that development in parallel with the evolution of the drug product. The goal and purpose of the method should reflect the phase of drug development. During early drug development the methods may focus on active pharmaceutical ingredient behavior.

2.11.2 Validation of Analytical Method:

Developed Method is validated according to the ICH Guidelines and data complying with the standards were obtained. All validation parameters were check for developed method. Validation parameter includes Accuracy, Precision, Specificity, Selectivity, Linearity, LOD, LOQ, and Robustness.

2.12. Following are the Markers used for method development by HPLC and HPTLC:

Table 3 Analytical markers for HPLC method

GALLIC ACID	OLEANOLIC ACID	E-Guggulsterone
		
Solubility: It is soluble in alcohol, ether, glycerol and acetone.	Solubility: It is soluble in Methanol	Solubility: It is soluble in Methanol, DMSO and Chloroform
Molecular weight: 170.12gm/mol	Molecular weight: 456.7 gm/ mol	Molecular weight: 312.453 gm/mol
Chemical Formula: C7H6O5	Chemical formula: C30H48O3	Chemical formula: C21H28O2

2.13. In Silico Method for screening of marker compounds for obesity

Over the past decades, many obesity drugs have been expelled due to serious side effects. this is why numerous studies are attentive on traditional medicine, which has remained Wide spread in all regions of the emerging world due to its powerful pharmacological activities, fewer side effects, and quite low cost. In significance, we have tried in this research to confirm the experimental results of plants known in the literature by computational chemistry techniques. (54)

The OB-receptor or leptin receptor (LR) is crucial for energy homeostasis and regulation of food uptake. Leptin is a 16 kDa hormone that is mainly secreted by fat cells into the bloodstream. Under normal circumstances, circulating leptin levels are proportionate to the fat body mass. Sensing of elevated leptin levels by the hypothalamic neuro-circuitry activates a negative feedback loop resulting in reduced food intake and increased energy expenditure.

In this study, we done molecular docking to identify therapeutic agents against obesity, and it is a technique that makes it possible to predict or study interactions that are the main factors having an important impact on the affinity of a ligand for a receptor. In addition, this study helps us to intend some plants as a treatment for weight loss.

Protein Selection:

Nine protein molecules were designated that are involved in the pathogenesis of obesity. The selected proteins, i.e., suppressor of cytokine signaling 3(Socs3), cholesteryl ester transfer protein (CETP), C-Jun N-terminal kinases-1(JNK1), lamin A/C, peroxisome proliferator-activated receptor γ (PPAR-γ), adiponectin, α-amylase, aldose reductase, and α-glucosidase

were retrieved from Research Collaboratory for Structural Bioinformatics (https://www.rcsb.org/) protein data bank. These modified proteins were then saved in the.pdb format.

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