CHAPTER-1

INTRODUCTION

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1.1 Introduction

Obesity is a health condition in which excess body fat has accumulated to the degree that it may have an side effect on health leading to reduced life expectation on health or increased health problems. Obesity is one of the major preventable causes of death in the world. Sedentary life style plays a key role in obesity. In one survey noted that, here has been a large shift towards less physical work and currently at least 60% of the world's population gets less exercise due to increased use of machine and other transportation. An average obesity reduces life anticipation by 6 to 7 years. Obesity is from lattin word obesitas, which means stout, fat or plump. The causes for obesity are high sugar intake, genetic disorder, GI disorder, stressful mentality and insufficient sleep [(1).] Obesity is condition which involves high amount of body fat, this fat store into the adipose tissues and other body parts like liver and muscles. It is stated by Body mass index. This is used to segregate person as underweight, overweight, normal or obese. BMI is ratio of person's weight in kilogram to the square of heights in meters. Obesity is a one of the major issue for increasing bad health problems. It leads to life threatening condition. [(2)] The obesity can be categorised into two ways: 1) High amount of fat, salt and sugar intake and same time less amount of less minerals, vitamins and other nutrients. 2) No physical activity or less physical activity because of more sedentary life style. Therefore the main reason behind the obesity is an imbalance between energy intake and output. Our body needs energy from diets for basic functions. When the energy expenditure is equal then body weight is maintained. [(3)]

Table 1.1 Body mass index chart

Less than 18.5	Underweight
18.5–24.9	Normal weight
25.0–29.9	Pre-obesity or Over weight
30.0–34.9	Obesity class I
35.0–39.9	Obesity class II
More than 40	Obesity class III

1.1.1 Etiology of obesity:

The global prevalence of obesity continues to rise at an alarming rate. Considerate the causes of excessive weight gain are really important, as it paves the way for the development of new therapies to control this epidemic. Obesity is a diverse chronic disease where so many reasons interact to produce a state of positive energy balance leading to an increase in body weight. The key biological factors include genetics, menopause, pregnancy, neuroendocrine

conditions, medications and physical disability. Propensity to develop obesity owing to one or more of these elements is exacerbated by environmental and behavioural influences. Environmental factors include food abundance, built environments, socioeconomic status, culture, social bias, and environmental chemicals. Behavioural factors include excessive food intake, eating patterns, sedentary lifestyles, insufficient sleep, smoking other addiction. It is essential to identify the determinants of adiposity in individuals with obesity to tailor prevention and treatment techniques effectively.

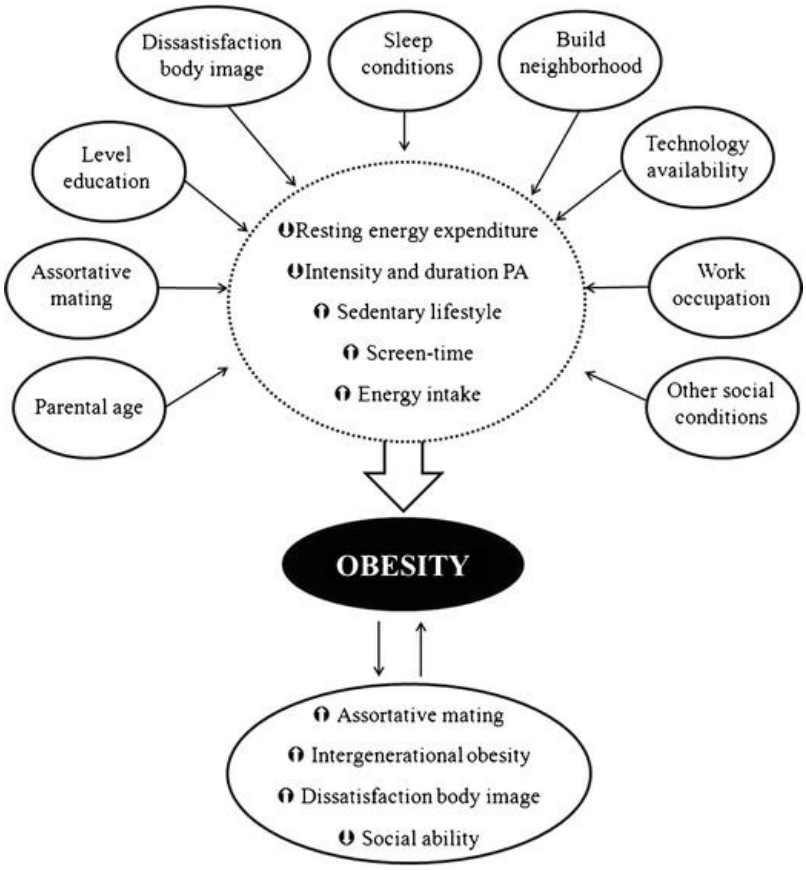

Figure 1.1Etiology of obesity

1.1.2 Epidemiology:

The epidemic of obesity presents a key task to chronic disease prevention and health across the life course everywhere in the world. Fuelled by economic growth, development, usage of transportation, an increasingly sedentary lifestyle, and a dietary transition to treated foods and high fat diets over the last many years, many countries have saw the prevalence of obesity in its citizens twice, and even more. Rising prevalence of childhood obesity, in particular, forebodes a staggering burden of disease in individuals and healthcare systems in the decades to come. A complex, multifactorial disease, with genetic, behavioural, socioeconomic, and

environmental origins, obesity raises risk of debilitating morbidity and mortality. Relying primarily on epidemiologic evidence published within the last decade, this non-exhaustive review discusses the extent of the obesity epidemic, its risk factors—known and novel—, squeal, and economic impact across the world..

1.1.3 Pathophysiology:

It is known that a disorder of the homeostatic mechanisms controlling energy balance causes obesity; it is less clear how the balance is concerned, since the mechanisms are very complex and involve in many systems in the body. Plasma leptin is more in obese subjects compared with normal weight individuals. In fact, leptin level are proportional to body fat mass in both obese and lean subjects. Thus, obesity is not due to the deficiency in circulating leptin. Resistance to leptin might be one of factors in development of obesity. Such resistance could be at the level of carriage of leptin in the circulation or its transport into the central nervous system. Defects in the leptin receptor (as in db/db m ice) or in the transducing system decreased expression of C RF or over expression of NPY could represent other disturbances in leptin system. Leptin exerts its anorexigenic action through its receptor, located in neurons of the infundibular nucleus of the hypothalamus. Activation of the leptin receptor will start a complex framework of system. These include a decreased secretion of neuropeptide Y, the most potent endogenous appetite stimulant.

Fat cells consist of 21-38% of total body weight of normal distinct; in case of obese people consumption of more calorie than the consumed and appetite cannot reduce to compensate the more storage of the fats. Adipose tissue is regulated by signals transmitted to brain. The imbalance between relocating a signal from adipose tissue to brain and response of brain to signals results in obesity. This system of energy stores will determine the food intake and energy expenditure. The mechanism include **Leptin** hormone secreted by adipose tissue, can give signals to brain about the amount of fat stores. Adipocyte-derived leptin modifies the suppression of appetite and increased energy outflow mediated by leptin signalling in hypothalamus. By contrast, stomach expresses both leptin and ObR, however, physiological significance of gastric leptin remains unclear. Table inside figure shows expression of leptin and ObR in the gastrointestinal tract.

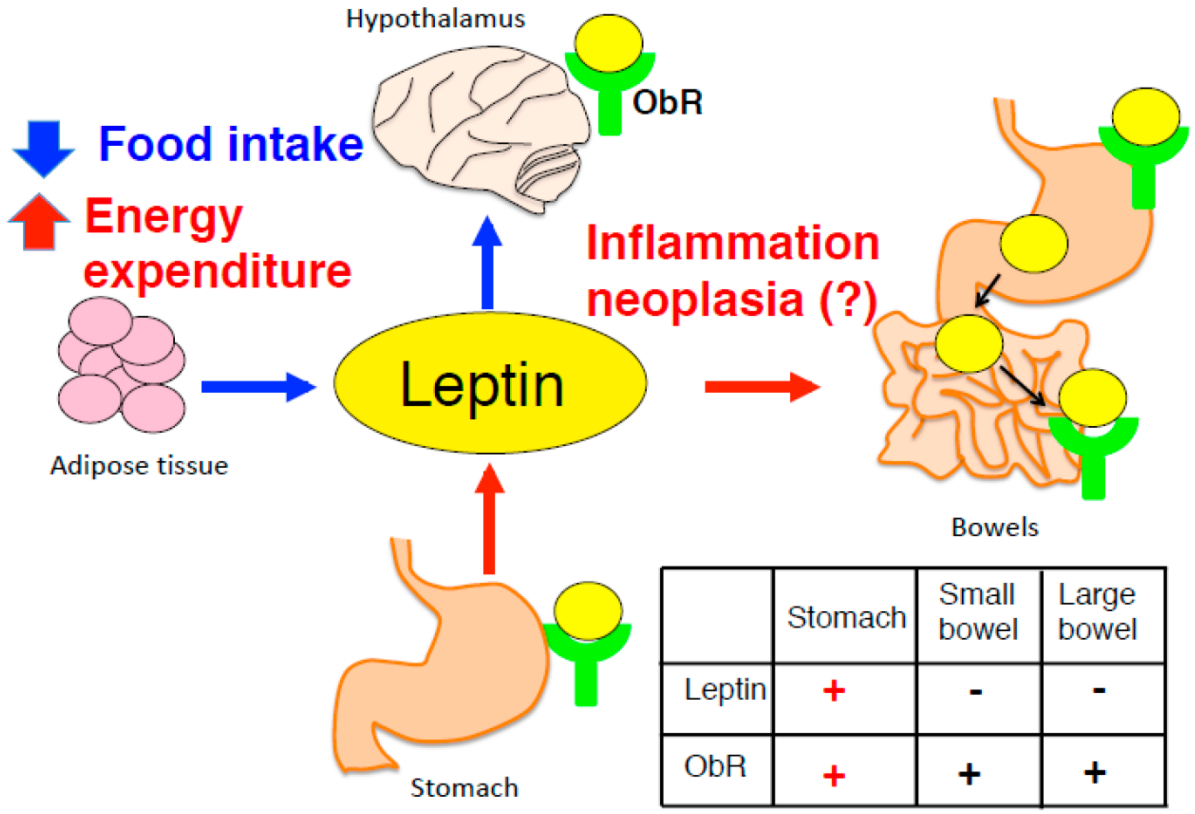

Figure 1.2Leptin and appetite

1.2. Causes of Obesity

A. Energy Balance in the Development of Obesity

Obesity can result from a slight energy imbalance, which lead to a gradual but determined weight gain over a significant period. Some researchers have hypothesized that energy imbalance is the result of inborn metabolic characteristics; whereas others believe it is caused by poor eating and lifestyle habits, that is “gluttony and sloth. Positive energy balance occurs when energy intake is greater than energy expenditure and promotes weight gain. Conversely, negative energy balance promotes decrease in body fat stores and weight loss. Body weight is regulated by a series of physiological processes, which have the capacity to maintain weight within a relatively narrow range (stable weight). It is thought that the body exerts a stronger defence against under nutrition and weight loss than it does against over-consumption and weight gain. Dietary intake and physical activity are important subsidizing factors in the development of obesity. If calorie intake is in excess of requirement it will be stored mainly as body fat. If the stored body fat is not utilised over time, it will lead to overweight or

obesity. Inter-individual distinctions in energy intake, basal metabolic rate, unstructured physical activity, the relative rates of carbohydrate-to-fat oxidation, and the degree of insulin sensitivity seem to be closely involved in energy balance and in defining body weight in some individuals.

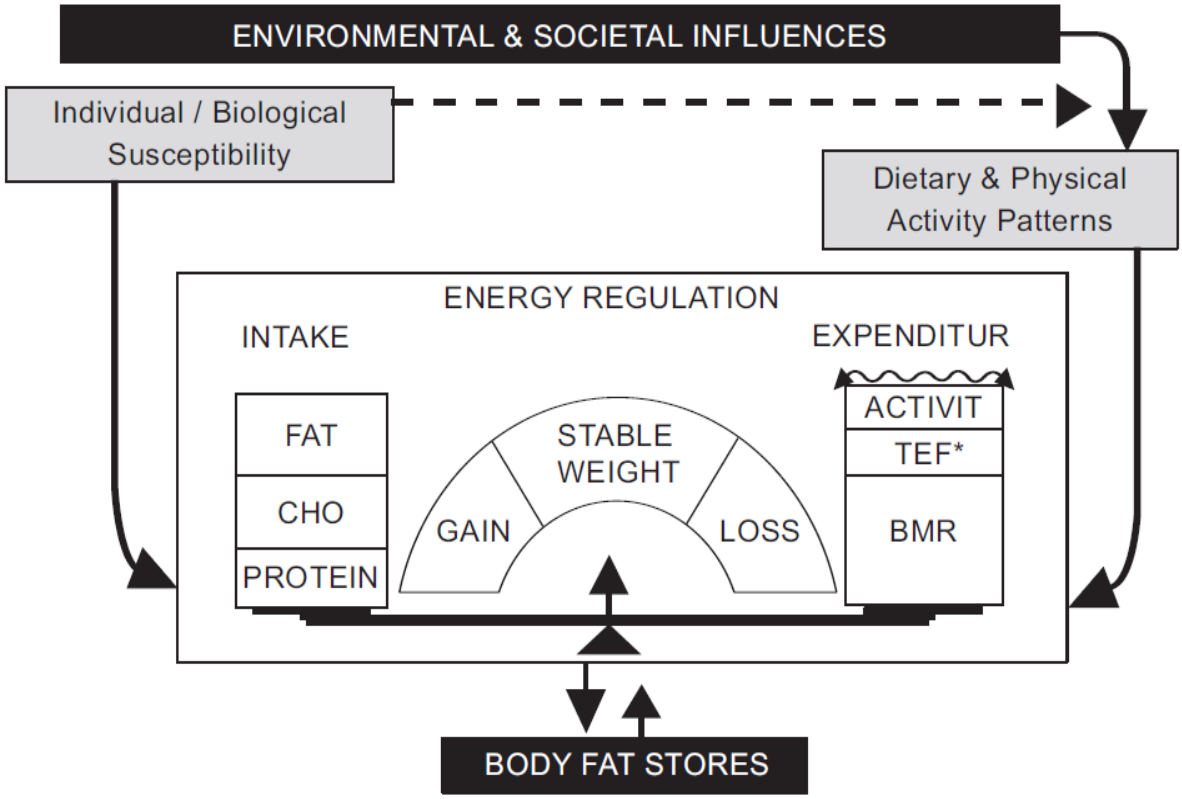

Figure 1.3Fundamentals of energy balance and energy regulation

Dietary Intake:

(A)**Food intake pattern:** FAO Food balance sheet data have shown that there has been a trend of increasing per capita convenience of the major macronutrients calories, fat and protein, particularly the protein and fat.

(B)**Macronutrient composition of the diet**: The association between energy intake and body weight relies on the ease with which excess macronutrients can be placed as adipose tissue. The energy cost of nutrient storage is not matching for all macronutrients. The cost of fat storage from dietary fat is the lowest, followed by carbohydrate and protein. Macronutrients with a low storage capacity such as protein and carbohydrate will be better oxidized when intakes exceeded requirements. Hence, excess dietary fat is more likely to be stored in the body and this capacity is unlimited. The caloric content of fat is also more than twice that of protein or carbohydrate.

(C)**High fat diets:** Foods or mealtimes that are high in fat are smaller in weight or volume than high carbohydrate foods or meals of similar energy content. Dietary fat content is

directly linked with energy intake, produces only weak satiation in comparison with protein and carbohydrate, and is assumed to be processed efficiently by the body. A number of studies found that individuals on a high-fat diet are more disposed to become overweight.

(D) **Energy dense foods and drinks:** Intense too much or too often high calorie foods and drinks may increase the total calories and thus result in obesity. The energy solidity of foods may be subsidised by its macronutrient contents. A high fat food will often be labelled as energy-dense. However, sugars for example table sugar, honey, syrups also fund to energy density.

(E) **Fibre content in the diet:** A diet with satisfactory amounts of fibre-containing foods is usually less energy dense. Its greater bulk has a short-term satiety effect, can help to prevent overeating and reduce risk of obesity. WHO endorses an intake of 20 to 30 grams of dietary fibre per day. This can be achieved by including fruits, vegetables, whole grain cereals, pulses and legumes in the diet. Efforts to increase dietary fibre intake should be gradual to minimize distress such as bloating and flatulence. It is important to drink a lot of water when increasing fibre intake.

(F) **Food palatability**: Palatability is defined as the brief subjective orosensory pleasantness of a food, which indicates the sensory stimulus to eat. It is one of the most powerful influences in helping calorie over-consumption (positive energy balance) by increasing both the rate of eating and the sense of hunger during and between meals. Perceived palatability of foods plays a major role in defining which foods are selected over others. It has also been argued that palatability is associated with the energy density of foods. Foods that are energy dense are more palatable than those of lower energy density. Fat is associated with palatability and gratifying mouth-feel that can induce behaviour which favours over-consumption leading to obesity.

1.3. Psychosocial Factors contributing to Obesity

Psychosocial factors take priority in terms of contribution to obesity because genetic changes do not occur quick enough to permit the increase of obesity cases around the world. Performance is governed by psychological aspects of human functioning, and is learnt through various experiences, including conditioning, reinforcements and modelling. Calorie intake and use largely depend on behaviour, which are food-related and non-food related. The significance of communicative factors in weight gain is that it can be modified more easily than genetics.

1. **Hunger and appetite:** Hunger is a functional response to a need for food triggered by stimuli acting on the brain. It can be affected by a number of factors such as the size and structure of preceding meal, habitual eating pattern, physical and mental states. Individuals who restrict food ingestion at each meal may feel extra hungry for a few days, but then hunger diminishes for a time. However, at some point of food withdrawal, hunger can be uncontrollable and lead to bouts of overeating that more than make up for the calories lost.

The stomach capacity can also adapt to larger food quantities and until a normal meal size no longer feel satisfying

2. **Food-related behaviour:** Humans have the ability to override signals of hunger and satiety and eat whenever they wish, especially when presented with situations that stimulate them to do so. Hence, overeating is a educated process with regards to modelling, conditioning and habituation. The main behavioural factors that contribute to obesity include:

- Excessive energy intake, and moderated rate of physical activity or energy output,
- Greater reaction to stimuli associated to food (especially energy dense food),
- Large bites of food and rapid eating – rapid eating allows greater amount of food to be spent before satiety signals are predictable.
- According to learning theories, certain types of food can be allied with certain pleasures, (e.g. eating while watching favourite TV program); or sets of personal beliefs, (e.g. the impropriety of wasting food).

Non-food-related behaviour: Non-food-related behaviour can also lead to obesity. These behaviours are sedentary behaviours such as sitting or sleeping for long hours, using lifts as compared to stair walking, driving to places that are within walking distance. In the modern world, mechanisms that reinforces sedentary behaviours include comfort in not moving much, discomfort when walking in hot and humid conditions, rewards for inactivity (e.g. being able to play computer games, having pleasant discussion, pleasant sleep), and punishment for over activity, especially in children. Many deskbound lifestyle promoting factors such as the television, mechanical transportation, computers and other labour-saving devices are increasingly available thus reducing the need for physical activity.

1.4. Remedies for obesity:

Pharmacological remedies for obesity:

Table 1.2Pharmacological Remedies

Sr. no	Drug Class	Mechanism of Action	Examples	Side effects
1	HMG COA reductase enzyme inhibitor	Lowering total LDL inhibiting cholesterol biosynthesis	Atrovastatins, Fluvastatin Lovastatin, Simvastatin	Congestive cardiac failure
2	Fibrates	Enhancing activity of enzyme lipoprotein lipase	Gemfibrozil, fenofibrate	Upper GI disturbance, headache, myalgia
3	Nicotinic acid derivative	Inhibit lipolysis within adipocytes	Niacin	Hyperglycemia. increase uric acid
4	Bile acid sequestrants	Bind with bile acid & promote bile acid excretion	Cholestipole, Cholestyramine	Abdominal fullness.

	(Resin)			constipation
5	Misc.	Inhibit free radicals	Omega 3 fatty acid, Probucol	

Prescription drugs for obesity:

Table 1.3Prescription drugs for obesity

Drug	Mechanism of Action	Side effects
Orlistat	Reduces fat absorption from the intestine by inhibiting pancreatic lipase and reduces triglyceride hydrolysis. Low fat diet is generally advised.	Steatorrhoea (oily stools).
Sibutramine	Centrally acting sympathomimetic amine that enhances satiety by inhibiting non- selective uptake of nor adrenaline, serotonin and dopamine	Hypertension, Serotonin syndrome
Metformin	It activates cAMP-activated protein kinase and suppresses hepatic gluconeogenesis activity.	Lactic acidosis, Gastro intestinal upset.
Rimonabant	It is an approved but infrequently used drug It is a canabinoid CB1 receptor antagonist. It predisposes selectively acts on CB1 receptor in brain and peripheral organs. Reduces lipogenesis in liver.	Severe depression and neurodegenerative diseases Eg Alzheimer's disease.

Herbal Remedies for the obesity:

Table 1.4Herbal Remedies for the obesity

Sr.no	Anti-obesity function	Herbs
1	Inhibiting pancreatic lipase activity	Chitosan,green tea
2	Enhancing thermo genesis	Sea Weed, Bitter Orange, Soybean
3	Preventing adipocyte differentiation	Turmeric, Capsicum, Palm Oil, Banana Leaf, Brown Algae, Garlic, Flaxseed, Black soybean, Kokam fruit
4	Enhancing lipid metabolism	Herb Teas, Cinnamon, Guggul Lipid
5	Decreasing appetite	Pine Nut, Pomegranate Leaf,Ginseng, Hoodia

		Gordonii, Aghedo, Methi Seeds

Marketed formulation for obesity:

Table 1.5Marketed formulation for obesity

Sr. No.	Name of Formulation	Composition
1	Ayurslim	Garcinia , Indian Bdellium Gymnema, Chebulic Myrobalan, Fenugreek
2	Trim	Garcenia, Pichrorriza Cuprus rotundus, Triphala

1.5. WHO Guidelines for Quality Assessment of Herbal Medicines

World health organization has recently defined traditional medicine as comprising therapeutic practices that have been in existence, often for hundreds of years, before the development and spread of modern medicine and are still in use in toady. The traditional preparations comprise medicinal plants, minerals, organic matter, etc. As per World Health Organization "Herbal Medicines" define as, "Finished, labelled medicinal products that contain as active ingredients aerial or underground parts of plants, or other plant material, or combinations thereof, whether in the crude state or as plant preparations. Plant material includes juices, gums, fatty oils, essential oils, and any other substance of this nature [(9)]

A method of identification and quantification of the plant material in the finished product should be defined. If the identification of an active principle is not possible, it should be sufficient to identify a characteristic substance or mixture of substances (e.g., “chromatographic fingerprint") to ensure consistent quality of the product[(10)]. Multicomponent botanical formulations can be standardized with newer techniques such as high pressure thin layer chromatography (HPTLC), liquid chromatography and mass spectroscopy. The value of animal testing to establish safety and toxicity is also critical for the botanicals used in traditional forms prepared using drugs with a narrow therapeutic index. Nevertheless, all the critical pharmacopoeial tests such as dissolution time, microbial, pesticide and heavy metals contamination etc. must be in accordance with global standards and all the herbal medicines manufactured must be in accordance with current good manufacturing procedures for herbs.

1.6. Quality of herbal products:

The quality of a plant product is determined by the prevailing conditions during growth, and accepted Good Agricultural Practices (GAP) can control this. These include seed selection, growth conditions, and use of fertilizers, harvesting, drying and storage. In fact, GAP procedures are, and will be, an integral part of quality control. Factors such as the use of fresh plants, age and part of plant collected, period, time and method of collection, temperature of processing, exposure to light, availability of water, nutrients, drying, packing, transportation of raw material and storage, can greatly affect the quality, and hence the therapeutic value of herbal medicines. Apart from these criteria, factors such as the method of extraction, contamination with microorganisms, heavy metals, and pesticides can alter the quality, safety, and efficacy of herbal drugs. Using cultivated plants under controlled conditions instead of those collected from the wild can minimize most of these factors. Sometimes the active principles are destroyed by enzymatic processes that continue for long periods from collection to marketing, resulting in a variation of composition. Thus proper standardization and quality control of both the raw material and the herbal preparations should be conducted [11].

1.7. Parameters for Quality Control of Herbal Drugs and Herbal products

- ✓ Microscopic Evaluation
- ✓ Determination of Foreign Matter
- ✓ Determination of Ash
- ✓ Determination of Heavy Metals
- ✓ Determination of Microbial Contaminants and Aflatoxins
- ✓ Determination of Pesticide Residues
- ✓ Determination of Radioactive Contamination

1.8. Standardization of Herbal Formulations

Standardization involves adjusting the herbal drug preparation to a defined content of a constituent or a group of substances with known therapeutic activity by adding excipients or by mixing herbal drugs or herbal drug preparations. Standardized extracts are high-quality extracts containing consistent levels of specified compounds, and they are subjected to rigorous quality controls during all phases of the growing, harvesting, and manufacturing processes. No regulatory definition exists for standardization of dietary supplements. As a result, the term “standardization” may mean many different things. Some manufacturers use

the term standardization incorrectly to refer to uniform manufacturing practices; following a recipe is not sufficient for a product to be called standardized. Therefore, the presence of the word "standardized" on a supplement label does not necessarily indicate product quality. When the active principles are unknown, marker substance(s) should be established for analytical purposes and standardization. Marker substances are chemically defined constituents of herbal drug that are important for the quality of the finished product. Single or multiple markers can be used to ensure that the concentration and ratio of components in an herbal mixture are present in reproducible levels in raw materials, manufacturing intermediates, and in the final dosage forms. In this way, multiple markers or chromatographic fingerprints give information assisting manufacturing control and assuring batch-to-batch consistency [(12)].

1.9. Medicinal Plants used for the treatment of obesity:

There are so many herbs and supplements are available in the market for the treatment of obesity. They all are having not same potential; purpose for use of herbs is they are having different way or mechanism to treat obesity. Many medicinal plants having direct or indirect role for the treatment of obesity like antioxidant, appetite suppression and increase the metabolism.

	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, roots and leaves	Ethyl acetate extarct of *A. calamus* inhibits α-glucosidase activity.
3	*Achyranthes bidentata* Blume (Amaranthaceae)	Root	The drug affects on differentiation of adipocyte and decrease 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 rootbarks	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 and4,11-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, SGOTand 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.

Table 1.6 List of the plant used in obesity

1.10 *In silico* Approach:

An in silico study is one executed via simulation on a computer. In silico simulations are frequently used to expect how a compound will react with proteins in the body or with pathogens.

Common applications for in silico studies include:

Drug candidate screening (molecular docking studies), Prediction of adverse drug reactions, Whole cell simulations and Sequencing (in silico PCR)

In silico models are computational simulations of a complex system in the form of comparisons or rules. In silico computational models provide the tools to qualitatively and quantitatively evaluate many treatments on specific diseases and to test a larger set of different conditions (e.g. dosing). These models are abstract representations used to model human diseases, a concept which is often limited by in-vitro/vivo techniques.

These types of models are becoming gradually popular within the pharmaceutical industry drug development especially. Computer-aided drug design (CADD), for example, is a group of in silico methods which deal a cost-effective way of finding drug candidates. The ligand-based design of CADD uses reference structures collected from the compounds known to interact with the target, and analyses their 2D/3D structure. [48]

Alternative of available biological evaluation methodology:

Computer-based models and tactics, like in silico, have the potential to lessen the number of animals needed in a study and maybe one day, replace them entirely. The shift from animal

models to computational versions has been a focus for the pharma industry for a number an important reasons.

- While animal models remain to show great value in preclinical studies, concern for the mental and physical well-being has seen a number of companies spread in alternative ways of modeling disease in order to reduce the number of animals used within drug development.
- The husbandry complicated with animals in research can be extensive, requiring large, expensive buildings for their maintenance with resources like food and frequent care required. In addition, some animal models can take a long time to progress which slows down the drug development process and again increases cost. Epilepsy rodent models, for example, can sometimes take up to a year to develop pathological variations in the brain before experiments can begin.

References:

1. Badri.N et al., A review: herbs used as anti-obesity agents. Indo American Journal of Pharm Research. 2011;1 nt of obesity. World journal of gastroenterology: WJG. 2009;15(25):3073.
2. Stroes ES et al. Statin-associated muscle symptoms: impact on statin therapy—European Atherosclerosis Society consensus panel statement on assessment, aetiology and management. European heart journal. 2015;36(17):1012-22.
3. Verma RK et at., Herbal medicines used in the traditional Indian medicinal system as a therapeutic treatment option for overweight and obesity management: A review. Int J Pharm Pharm Sci. 2014;6:40e7.
4. Jebb SA et al., Contribution of a sedentary lifestyle and inactivity to the etiology of overweight and obesity: current evidence and research issues. Medicine and science in sports and exercise. 1999;31(11 Suppl):S534-41.
5. Schoeller DA. The importance of clinical research: the role of thermogenesis in human obesity. The American journal of clinical nutrition. 2001;73(3):511-6.
6. Gurevich-Panigrahi T et al., Obesity: pathophysiology and clinical management. Current medicinal chemistry. 2009;16(4):506-21
7. WHO. Guidelines for the Assessment of Herbal Medicines. WHO Technical Report Series, No 863. World Health Organization, Geneva, 1996.
8. EMEA. Guidelines on Quality of Herbal Medicinal Products/Traditional Medicinal Products, EMEA/CVMP/814OO Review. European Agency for the Evaluation of Medicinal Products (EMEA), London, 2005
9. Blumenthal M, Brusse WR, Goldberg A, Gruenwald J, Hall T, Riggins, CW, Rister, RS. The Complete German Commission E Monographs. Therapeutic Guide to Herbal Medicines. The American Botanical Council, Austin, TX, 1998.
10. Bandaranayake WM. Quality Control, screening, toxicity and regulations of Herbal drugs. In: Modern Phytomedicine: Turning medicinal plants into drugs. pp. 25-57,2006.
11. Witkamp RF. Current and future drug targets in weight management. Pharmaceutical research. 2011;28(8):1792-818.
12. Ikarashi N, et al.., Anti-obesity and anti-diabetic effects of acacia polyphenol in obese diabetic KKAy mice fed high-fat diet. Evidence-Based Complementary and Alternative Medicine. 2011;2011.

13. Rani N, Sharma SK et al.,. Assessment of antiobesity potential of Achyranthes aspera Linn. seed. Evidence-Based Complementary and Alternative Medicine. 2012;2012.
14. Subash AK, et al.Hypolipidemic effect of methanol fraction of Aconitum heterophyllum wall ex Royle and the mechanism of action in diet-induced obese rats. Journal of advanced pharmaceutical technology & research. 2012;3(4):224.
15. Lee M-H et al.,Inhibitory effect of β-asarone, a component of Acorus calamus essential oil, on inhibition of adipogenesis in 3T3-L1 cells. Food chemistry. 2011;126(1):1-7.
16. Kumar R et al.,. Invitro studies on the effect of adhatoda vasica nees. In adipocyte 3t3-l1 cell lines. 2017.
17. Kim I et al.,. Beneficial effects of Allium sativum L. stem extract on lipid metabolism and antioxidant status in obese mice fed a high-fat diet. Journal of the Science of Food and Agriculture. 2013;93(11):2749-57.
18. Misawa E et al. Administration of dried Aloe vera gel powder reduced body fat mass in diet-induced obesity (DIO) rats. Journal of nutritional science and vitaminology. 2012;58(3):195-201.
19. Kumaraswamy M et al., Free radical scavenging activity and lipoxygenase inhibition of Woodfordia fructicosa Kurz and Betula utilis Wall. African Journal of Biotechnology. 2008;7(12):2013.
20. Kumar A et al., Antihyperlipidemic activity of Camellia Sinensis leaves in triton wr-1339 induced Albino rats. Pharmacognosy magazine. 2008;4(13):60.
21. Kremmer T et al., Effect of Vincristine on Triton WR-1339 induced hyperlipidemia in mice. Biochemical pharmacology. 1974;23(23):3317-21.
22. Chithra V et al., Hypolipidemic effect of coriander seeds (Coriandrum sativum): mechanism of action. Plant Foods for Human Nutrition. 1997;51(2):167-72.
23. Patil UK et al., Hypolipidemic activity of seeds of Cassia tora Linn. Journal of ethnopharmacology. 2004;90(2):249-52.
24. Patil S et al., Antihyperlipidemic potential of Cedrus deodara extracts in monosodium glutamate induced obesity in neonatal rats. Indian journal of pharmacology. 2011;43(6):644.
25. Bhandari U et al., Antidiabetic effects of Embelia ribes extract in high fat diet and low dose streptozotocin-induced type 2 diabetic rats. Frontiers in Life Science. 2013;7(3-4):186-96.

26. Gopa B et al., A comparative clinical study of hypolipidemic efficacy of Amla (Emblica officinalis) with 3-hydroxy-3-methylglutaryl-coenzyme-A reductase inhibitor simvastatin. Indian journal of pharmacology. 2012;44(2):238.
27. Darji KK et al., Evaluation of antioxidant and antihyperlipidemic activity of extract of Garcinia indica. Int J Pharm Sci Res. 2010;1(12):175-81.
28. Rachh P et al. Antihyperlipidemic activity of Gymenma sylvestre R. Br. leaf extract on rats fed with high cholesterol diet. IJP-International Journal of Pharmacology. 2010;6(2):138-41.
29. Ali KM et al., Attenuation of diabetic disorders in experimentally induced diabetic rat by methanol extract of seed of Holarrhena antidysenterica. Int J PharmTech Res. 2009;1:1205-11.
30. Hossain M et al., Hypolipidemic and hepatoprotective effects of different fractions of methanolic extract of Momordica charantia (Linn.) in alloxan induced diabetic rats. International Journal of Pharmaceutical Sciences and Research. 2011;2(3):601.
31. Bais S et al., Antiobesity and hypolipidemic activity of Moringa oleifera leaves against high fat diet-induced obesity in rats. Advances in Biology. 2014;2014.
32. Kumar G et al., The hypolipidemic activity of Ayurvedic medicine, Arogyavardhini vati in Triton WR-1339-induced hyperlipidemic rats: A comparison with fenofibrate. Journal of Ayurveda and integrative medicine. 2013;4(3):165.
33. Bao L et al., Hypolipidemic effects of a new piperine derivative GB-N from Piper longum in high-fat diet-fed rats. Pharmaceutical biology. 2012;50(8):962-7.
34. Vijayakumar RS, Nalini N. Lipid-lowering efficacy of piperine from piper nigrum l. In high-fat diet and antithyroid drug-induced hypercholesterolemic rats. Journal of food biochemistry. 2006;30(4):405-21.
35. Pendurkar SR, Mengi SA. Antihyperlipidemic effect of aqueous extract of Plumbago zeylanica roots in diet-induced hyperlipidemic rat. Pharmaceutical biology. 2009;47(10):1004-10.
36. Sadeghipour A et al., Lipid lowering effect of Punica granatum L. peel in high lipid diet fed male rats. Evidence-Based Complementary and Alternative Medicine. 2014;2014.
37. Maruthappan V, Shree KS. Hypolipidemic activity of Haritaki (Terminalia chebula) in atherogenic diet induced hyperlipidemic rats. Journal of advanced pharmaceutical technology & research. 2010;1(2):229.

38. Shaila H et al., Hypolipidemic activity of three indigenous drugs in experimentally induced atherosclerosis. International journal of cardiology. 1998;67(2):119-24.
39. Israni DA et al., Anti-hyperlipidemic activity of aqueous extract of Terminalia chebula & Gaumutra in high cholesterol diet fed rats. Pharma science monitor. 2010;1(1):48-59.
40. Meriga B et al., Ethanolic fraction of Terminalia tomentosa attenuates biochemical and physiological derangements in diet induced obese rat model by regulating key lipid metabolizing enzymes and adipokines. Pharmacognosy Magazine. 2017;13(51):385.
41. Yang M-H, et al., Green, oolong and black tea extracts modulate lipid metabolism in hyperlipidemia rats fed high-sucrose diet. The Journal of nutritional biochemistry. 2001;12(1):14-20.
42. Kammar K. Efficacy of Tinospora cordifolia (Willd.) extracts on blood lipid profile in streptozotocin diabetic rats. Is it beneficial to the heart? Biomedical research. 2008;19(2).
43. Javed I et al. Antihyperlipidaemic efficacy of Trachyspermum ammi in albino rabbits. Acta Veterinaria Brno. 2009;78(2):229-36.
44. Khan S et al., Antihyperlipidemic potential of fruits of Tribulus terrestris linn. Int J BiomedRes. 2011;2:98-101.
45. Prasanna M. Hypolipidemic effect of fenugreek: a clinical study. Indian journal of Pharmacology. 2000;32(1):34-6.
46. CHEN C-y et al., Effect of the Extract of Valeriana jatamansi on the Blood Lipid and Liver Function in Experimental Hyperlipidemia Rats. Chinese Journal of Experimental Traditional Medical Formulae. 2012;19:046.
47. ElRokh E-SM et al., Antihypercholesterolaemic effect of ginger rhizome (Zingiber officinale) in rats. Inflammopharmacology. 2010;18(6):309-15.
48. Mandar BK et al., In silico analysis of phytoconstituents from Tinospora cordifolia with targets related to diabetes and obesity. In Silico Pharmacol. 2021 Jan 2;9(1):3. doi: 10.1007/s40203-020-00063-w. PMID: 33442530; PMCID: PMC7778662.