

## Review Article



## Effects of *Camellia sinensis* and *Garcinia cambogia* on obesity & its comorbidities – safer alternative then synthetic drugs

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### ABSTRACT

In the current scenario obesity is one of the major concerns in the world population. Its prevalence is reached global epidemic proportions which shown has its effect in many developing countries. In 2012, there are around 46.6% of obese male & 70.3% female. Obesity which is associated with serious health risks & cause high rate of mortality. Its morbidities are atherosclerosis, fatty liver, hyperlipidemia, Diabetes Mellitus and various types of cancer. The synthetic drugs such as sibutramine, rimonabant, orlistat and phentramine which are used in treatment of obesity have some adverse effects. The most serious adverse effects are cardiovascular events so that's why natural herbs have become a safer alternative treatment for obesity. The herbal plants which are widely used for the management of obesity are *Achyranthus aspera*, *Aloe barbedenosis*, *Citrus sinensis*, *Ephedra vulgaris* etc. *Garcinia cambogia* and *Camellia sinensis* extract has also showed antiobesity activity in animal studies. This review focuses on the potential of their use in treatment of obesity.

**Keywords:** hydroxycitric acid, metabolic, cardiovascular, epigallocatechin.

### INTRODUCTION

In many countries the incidence of obesity is increasing at an alarming rate during the past few years, it has reached epidemic proportions & is a major contributor to the global burden of chronic disease. Approximately 200,000 individuals throughout the world die every year. It is also affecting younger children and adolescent. It is already reported that approximately 61% adults are overweight and 28% obese, 14% adolescents and 13% children in the age 6 to 8 are overweight<sup>1</sup>.

Obesity is a metabolic disorder in which excess body fat has accumulated to the extent that it may lead to major health problems. It is the result of taking in more calories in the diet than are expected by the body's energy-consuming activities. Body mass index (BMI), a measurement which compares weight and height, defines people as overweight (pre-obese) if their BMI is between 25 and 30 kg/m<sup>2</sup>, and obese when it is greater than 30 kg/m<sup>2</sup>. The body can convert excess fuel to fat and store it in adipose tissues, or it can burn excess fuel by extra exercise and in another way it can waste fuel by diverting it to producing heat in uncoupled mitochondria. In mammals a complex set of hormonal and neuronal signals act to keep fuel intake and energy expenditure in balance<sup>2</sup>.

Obesity is multifactorial. It is related with numerous factors like behavioural, environmental and genetic factors. These are related with dysregulation of energy homeostasis which is maintained by hypothalamus<sup>3</sup>. Weight gain occurs from the disruption of the normal homeostatic functioning of the hypothalamic centres which are responsible for controlling satiety and hunger and in regulating energy balance with which results in

hyperphagia, autonomic imbalance, reduction of energy expenditure, and hyperinsulinemia<sup>4</sup>.

### Role of hypothalamus and gut hormones in obesity:

The hypothalamus consists of several nuclei that integrate peripheral signals, such as adiposity and caloric intake, to regulate important pathways within the CNS controlling food intake. The best characterized pathways are the orexigenic neuropeptide Y/Agouti-related protein and the anorexigenic pro-opiomelanocortin/cocaine- and amphetamine-related transcript neurons in the nucleus of the hypothalamus. These neuropeptides have an important role in regulation of lipid metabolism and obesity. There are also projections to and from the brainstem, cortical areas and reward pathways, all of which influence food intake. The challenge at present is to understand the complexity of these pathways and try to find ways of modulating them in order to find potential therapeutic targets. There are series of complex systems which regulate energy homeostasis so that sufficient energy is available and bodyweight remains stable. Central circuits in the brain rely basically on peripheral signals indicating satiety levels and energy stores, as well as higher cortical factors, such as emotional and reward pathways. The hypothalamus is critical in the regulation of food intake and acts as a 'key controller' within neural circuitry to maintain energy homeostasis. The hypothalamus is an integral part of the processing of afferent signals, such as those from the gut and brainstem, as well as the processing of efferent signals that modulate food intake and energy expenditure. Gut hormones acting via vagal afferents act on the brainstem, which in turn sent signals to the hypothalamus. Some gut hormones may also act directly on hypothalamic nuclei via the circulation and across an incomplete blood-brain



barrier. There are projections which extend from hypothalamic nuclei to the prefrontal cortex, involved in conditioned taste aversion, as well as reward centres, such as the amygdala and nucleus accumbens.

Leptin is also thought to act directly on the nucleus tractus solitarius as well as hypothalamic nuclei, proposing that it can modulate appetite through different pathways. It is a key adipokine secreted by adipocytes in proportion to fat mass, signals to the central nervous system regarding the status of fat stores to control food intake.

Ghrelin is a gastric hormone that plays a role in long-term and short-term energy balance and acts centrally to increase food intake. It reaches its maximal plasma levels before meals in order to stimulate food intake. After the meal its levels are reduced to its lowest point. The consumption of high calorie diet and soft drinks are the major risk factors for obesity. It is necessary to understand the various signals and their interactions that contribute to obesity.

### CCK

Cholecystokinin (CCK), a peptide that is distributed widely throughout the gastrointestinal tract and the central nervous system, has a number of physiological effects including the stimulation of gallbladder contraction, pancreatic and gastric acid secretion, slowing of gastric emptying and suppression of energy intake<sup>5</sup>. It belongs to the group of substances known as brain-gut peptides. It functions both as a neuropeptide and a gut hormone. The peptide and its synthetic derivatives (like for instance CCK-8 and the amphibian counterpart caerulein) significantly delay emptying of gastric contents in both animals and humans. The fact that CCK, in doses mimicking postprandial plasma levels, strongly affects emptying rate suggests the peptide to be a physiologic regulator of gastric emptying<sup>6</sup>.

The variety of CCK's physiologic effects emphasizes its integrative function on both digestive and metabolic processes. After a meal, CCK

(1) Regulates the movement of nutrients through the gastrointestinal tract

(2) Contracts the gallbladder and stimulates pancreatic exocrine secretion to facilitate digestion.

(3) Potentiates amino acid-induced insulin secretion and delays gastric emptying to maintain euglycemia.

An effect to reduce food intake following food ingestion would be a logical extension of these integrated actions. Thus, CCK appears to have an essential role in regulating the intake, processing, and distribution of essential nutrients<sup>7</sup>.

### Risk factors

Some of the patients are more prone to high risk. These patients are at high risk for subsequent mortality. Some of the high risk morbidities are as follows:

- 1) Established coronary heart disease, atherosclerotic diseases, DM-2, and sleep apnea.
- 2) Three or more of the following are considered high risk.
  - A. Hypertension.
  - B. Cigarette smoking.
  - C. High low-density lipoprotein cholesterol (LDL-C).
  - D. Low high-density lipoprotein cholesterol (HDL-C).
  - E. Impaired fasting plasma glucose.
  - F. Family history of early cardiovascular disease, and age (male 45 years, female 55 years).
- 2) Other disease condition that denote absolute high risk but not considered generally life threatening.
  - a. Osteoarthritis.
  - b. Gallstones.
  - c. Stress incontinence.
  - d. Gynaecological.

### Therapeutic targets on obesity

The development of effective pharmacological therapies has been both the greatest hope and one of the greatest disappointments in the field of obesity. At its root, obesity is a complex, but ultimately understandable, metabolic and behavioural disorder that disrupts normal body weight regulatory mechanisms. Management of obesity is a difficult challenge because of the prevailing unfavourable lifestyle. There is available effective treatments to prevent obesity. The predominant goal of therapy currently is to reduce the complication of obesity. The drugs used for obesity have some adverse effect that can cause serious complications.

Clinical criteria for pharmacological therapy for obesity

- Body mass index (BMI) > 30 kg/m<sup>2</sup> or BMI > 27 kg/m<sup>2</sup> in Association with significantly medical complications.
- Failure of behavioural approaches, including diet and exercise Regimens.
- No strong contraindications to the medication used.

### Pharmacological treatment for obesity

Synthetic drugs are emerging therapy for treatment of obesity although they have some side effects some are also withdrawn from the market. However therapies targeting on weight loss have history of safety risks which includes cardiovascular and psychiatric events. Some are approved by FDA, sibutramine and orlistat are approved medications for treatment of obesity. Orlistat is a lipase inhibitor which deactivates intestinal lipase and also inhibits lipolysis. It is actually a drug on European market approved for the treatment of obesity. Malabsorption, steatorrhea is some side effects of orlistat. Orlistat also



reduce the incidence of diabetes<sup>8</sup>. Sibutramine is a centrally acting serotonin/nor adrenaline reuptake inhibitor that mainly increases satiety. Sibutramine in patients taking serotonin-selective reuptake inhibitors (SSRI) is relatively contraindicated because of the risk of serotonin syndrome.

It is not recommended in patients with history of cardiovascular disease and uncontrolled hypertension<sup>9</sup>.

The use of Phentramine, sibutramine or Bupropion in patients taking monoamine oxidase inhibitors (MAOIs) is strongly contraindicated because of the risk of severe cardiovascular events. Sibutramine in patients taking serotonin-selective reuptake inhibitors (SSRI) is relatively contraindicated because of the risk of serotonin syndrome.

#### a. Approved by the FDA specifically for weight loss indication

Medication	Typical dosing	Classification	Common adverse effect
Phentramine	15–37.5 mg per day	Adrenergic agent	Tachycardia, hypertension
Sibutramine	10–15 mg one per day	Serotonergic/adrenergic	Serotonergic/adrenergic, Hypertension, tachycardia
Orlistat	120 mg three times daily	Lipase inhibitor	Malabsorption, steatorrhea

#### b. Approved by FDA for indication

Medication	Typical dosing	Classification	Common adverse effect
Bupropion	150–300 mg/per day	Depression	Anticholinergic, agitation
Metformin	500-1000 mg/per day	Type 2 diabetes	Hepatic oxidative injury
Topiramate	50-100 mg/per day	Seizure disorder	Cognitive impairment
Zonisamide	400-600mg/per day	Seizure disorder	Cognitive impairment

### Obesity and its manifestations

As it is stated before that obesity is related to other metabolic disorder .it is a medical condition where excess fat is accumulated in adipose tissue which decreases the probability of life expectancy and escalated the risk of other health problems.

Adipose tissue (AT) is the most active organ and also the main energy store of body. It is an endocrine organ in which excess fat is stored and this leads to chronic inflammation which increases the risk of metabolic dysfunction in development of obesity. When lack of proportion occurs between energy expenditure and food intake it leads to serious conditions including insulin resistance, non-alcoholic fatty liver disease and all these pathological condition are inter related with each other. AT has an endocrine role, secreting many different adipokine and cytokines into the circulation that have an impact on whole body physiology in significant ways.

Free fatty acids (FFA) releases from excessive fat stored in endocrine organ, It also have most important role in insulin resistance. However plasma free fatty acids level do not increase the proportion to amount of body fat since there adipose tissue lipolysis per kilogram of fat is lower in obese than in lean subjects. Obesity is associated with elevated levels of proinflammatory cytokines and chemokines in the circulation and in tissues<sup>12</sup>. The adipose tissue produces and releases a large number of cytokines and chemokines (collectively called adipokine)<sup>13</sup>, some of which are proinflammatory. Recent studies have given emphasis on the reasons for the increased release of proinflammatory cytokines in obesity. In one study, mice fed a high fat diet for 3

months developed low grade hepatic inflammation which was associated with increased production and secretion of several proinflammatory cytokines<sup>10</sup>. This suggested that the inflammatory state was caused either by a component of the diet or by a substance released from the enlarged adipose tissue. FFA is good candidates for both possibilities because they are elevated in most obese individuals both during a fat meal<sup>11</sup> and under basal and postprandial conditions<sup>12</sup>. Macrophages are mononuclear phagocytic cells that are part of the innate immune system, an evolutionarily conserved defence system with cells placed at ports of entry of pathogens and other environmental threats to the body<sup>13</sup>.

Obesity is also associated with increased adipose tissue macrophage (ATM) infiltration, and rodent studies suggest that inflammatory factors produced by ATMs contribute to insulin resistance and type 2 diabetes. However, a relationship between ATM content and insulin resistance has not been clearly established in humans<sup>14</sup>. Subsequent studies have demonstrated that macrophage infiltration into white AT is increased in obesity<sup>15</sup>. Macrophages infiltration undergoes inflammation through these three stages initiation, propagation, remodelling in adipose tissue.

Pro-inflammatory T-lymphocytes are present in visceral adipose tissue and may contribute to local inflammatory cell activation before the appearance of macrophages, suggesting that these cells could play an important role in the initiation and perpetuation of adipose tissue inflammation as well as the development of insulin resistance. Previous studies have shown that macrophage infiltration is of critical importance in adipose tissue



inflammation and the development of insulin resistance<sup>16</sup>. This macrophage infiltration can alter other metabolic factors by inflammation and can have effect on insulin resistance. Macrophages are mononuclear phagocytes. They reside within almost all tissues, where they are identifiable as distinct populations with tissue-specific morphologies, localizations, and functions. In pathophysiology of obesity macrophages infiltration and T lymphocytes infiltration contributes to inflammation in adipose tissue. Inflammation can also leads to the development of diabetes mellitus and arteriosclerosis.

### **Obesity complication with dyslipidemia, non alcoholic fatty liver disease**

Dyslipidemia is an abnormal amount of lipids, such as cholesterol and triglyceride, in the blood and is a widely accepted risk factor for cardiovascular disease. Obesity-related dyslipidemia is primarily characterized by increased levels of plasma free fatty acids and triglycerides, decreased levels of high-density lipoprotein (HDL), and abnormal low-density lipoprotein (LDL) composition<sup>17</sup>. The pathophysiology of the typical dyslipidemia observed in obesity is multifactorial and includes hepatic overproduction of VLDL, decreased circulating TG lipolysis and impaired peripheral FFA trapping, increased FFA fluxes from adipocytes to the liver and other tissues and the formation of small dense LDL. Dyslipidemia raises hyper triglycerides level which increases the probability of cardiovascular diseases.

It is a widely accepted risk factor for coronary heart disease<sup>18</sup>. The dyslipidemia associated with obesity no doubt plays a major role in the development of atherosclerosis and cardiovascular risk, a life threatening diseases in obese individuals. Lifestyle modifications, weight loss and exercise, dietary fibres and with weight loss medications can improve this dyslipidemia reducing cardiovascular risk.

Obesity is also associated with increased risk factor of non alcoholic fatty liver disease (NAFLD). It has become a major health problem more prevalent at present because it is associated with other cardiovascular abnormalities. Currently it is the most chronic form of liver disease. Steatosis is the hallmark feature of NAFLD; it occurs when the rate of hepatic fatty acid uptake from plasma and de novo fatty acid synthesis is greater than the rate of fatty acid oxidation and export as triglyceride within very low density lipoprotein. The presence of steatosis is associated with a various adverse changes in glucose, fatty acid and lipoprotein metabolism. NAFLD is considered to be the hepatic manifestation of metabolic syndrome and is usually related to high cholesterol diets<sup>19</sup>.

As obesity is associated with many other metabolic disturbances such as insulin sensitivity, dyslipidemia, NAFLD. Adipose tissue dysfunction results in infiltration of macrophages and T lymphocytes and the imbalance between proinflammatory and anti-inflammatory factors which leads to the development of inflammation,

deterioration of insulin sensitivity and impairment of lipid metabolism. Free fatty acids also increases the other obesity related complications.

### **Herbal drugs as antiobesity drugs**

#### ***Garcinia cambogia***

*Garcinia cambogia* (GC), a fruit native to south-eastern Asia and Western Africa, has beneficial effects on body weight and fat loss in both experimental animals and human [6-10]. Its main component is hydroxycitric acid (HCA) which not only inhibits ATP-citrate lyase, the enzyme response for de novo fatty acid synthesis, but also increases hepatic glycogen synthesis, reduces food intake by suppressing appetite and decreases body weight gain<sup>20</sup>.

The genus *Garcinia* includes more than 300 species and belong to the family clusiacea .the plant of genus have various applications in pharmaceutical industries .It is also present in some ayurvedic preparations in combination and alone for curing various pathophysiological disorders. It is marketed as Super citrimax<sup>R</sup> as a weight loss supplement .It is a calcium, potassium salt of (-) hydroxycitric acid which is isolated from the fruit rind of *Garcinia cambogia*. It also enervated the increase in oxidative stress inflammation, insulin resistance and effect on body weight in developing obese zucker rats<sup>21</sup>. HCA is a highly unstable salt of and therefore extracted as a salt of preferably as calcium or potassium. The plant contains various chemical constituents such as xanthones, benzophenones, garcinol and plants acids like hydroxyl citric acid, malelic acid, citric acid. The fruit of *Garcinia cambogia* has been used traditionally used in food preparation and cooking as a flavouring agent .It had gathered a lot of attention as natural weight loss aid. The fruit rind of *Garcinia cambogia* combined with salts and other organic acid can help to lower the pH thus it also provides a bacteriostatic effect in curing fish<sup>22</sup>.

#### **Active constituent of *Garcinia cambogia***

The main constituent hydroxyl citric acid of *Garcinia cambogia* has gathered reputation for using as a weight loss aid through two mechanisms appetite suppression and by reducing the body's ability to form adipose tissue. It inhibits an enzyme that helps to synthesize body fat body for storage in adipose tissue. It promotes energy which inhibits lipogenesis and lowers the production of cholesterol and fatty acids. It increases the glycogen level in the liver and increases the body's production of heat by activating the process thermogenesis<sup>23</sup>.

In appetite suppression process HCA inhibits the enzyme ATP citrate lyase. It is an extra mitochondrial enzyme which is involved in catalyzing the cleavage of citrate to oxaloacetate and acetyl COA<sup>23</sup>. Finally the availability of two carbon units was limited which is needed during the beginning of fatty acid synthesis and cholesterol synthesis as a result consumed carbon source was diverted to glycogen synthesis in liver . Then a signal was sent to the



brain due to its change in metabolic system which results in the serotonin concomitant level<sup>24</sup>. Previously a study was conducted in obese rats which have reported that HCA caused a significant reduction in appetite weight loss, plasma Leptin level, concomitant with an increase in serum serotonin level<sup>25</sup>. Its mechanism also involvement of serotonin for appetite suppression.

Serotonin plays an important role in regulation of appetite and feeding behaviour.

It was first established in the 1970s that the brain serotonin (5-HT) system was involved in the control of eating. Nowadays molecular pharmacology has become more advanced in the development of selective 5HT receptor ligands. It has clarified the role of 5HT in the regulation of appetite<sup>26</sup>. Hydroxy citric acid is also acts on 5HT ligands as, it interfere with the pathways of 5HT which send signals to brain.

### Denovo lipogenesis

In pathophysiology of obesity as mentioned earlier free fatty acids circulate in vasculature and produce oxidative stress by circulating throughout the body. The release of these excessive fatty acids then instigates lipotoxicity as lipids and there metabolite and generate oxidative stress to endoplasmic reticulum and mitochondria. This lipotoxicity causes insulin receptor dysfunction by release free fatty acids by endothelial lipoprotein lipase from increased serum triglycerides within elevated beta protein lipase.

Lipotoxicity also decreases the secretion of pancreatic beta cell insulin which progressively results in beta cell exhaustion<sup>27</sup>.

HCA interferes with the process of lipogenesis as it reduces the acetyl COA thus it diminishes the availability of building blocks which is required for fatty acid and cholesterol synthesis. HCA inhibit lipogenesis where acetyl COA is converted to fatty acids which prevent fatty acids to cause lipotoxicity<sup>28</sup>.

(-)-Hydroxycitrate (HCA) might promote weight maintenance by limiting the capacity for de novo lipogenesis (DNL). It was investigated whether HCA may reduce DNL in humans during a persistent excess of energy intake as carbohydrate. Randomized controlled clinical trial was conducted which proved this that it have some effect on body weight gain<sup>29</sup>. HCA might also induce satiety by inhibiting malonylCoA formation, which in turn would stimulate carnitine transferase activity, resulting in decreased fat synthesis and increases fat oxidation<sup>30</sup>.

HCA administration has been shown to inhibit the rate of lipogenesis in rodents<sup>31</sup> and in increasing the rate of hepatic glycogen synthesis<sup>32</sup> but this has not been confirmed in humans, as there is a requirement of carbohydrate during de novo lipogenesis and to increase the glycogen synthesis.

### Commercial products of *Garcinia cambogia*

Super citrimax<sup>R</sup> is a novel calcium potassium salt of (-) hydroxycitric acid which is a commercial product of *Garcinia cambogia* and commonly consumed as weight loss dietary supplement. Researchers has concluded that Super citrimax<sup>R</sup> has decreases the food intake, body weight gain and also attenuates the increase in inflammation, oxidative stress, and insulin resistance<sup>33</sup>. HCA (as Super Citrimax<sup>R</sup>) has been generally recognized as safe (GRAS) by the Burdock Group, one of the nation's leading food ingredient safety and toxicology groups<sup>34</sup>.

### Toxicology profile of *Garcinia cambogia*

Hydroxy citric acid, active component of *Garcinia cambogia* is widely used as a weight loss supplement. Its toxicological profile not shows the sign of liver toxicity and in promotion of inflammation but studies on animal has concluded that *Garcinia cambogia* extract have found it to reduce markers of inflammation in brain, intestines, kidney and serum and to be either protective or neutral in terms of liver health<sup>35</sup>. The recent data shows that hydroxycitric acid does not cause liver toxicity. The data reported by Kim *et al* that a *Garcinia cambogia* extract (GC, 1%, w/w) fed to C57BL/6J mice in conjunction with a high-fat diet (HFD, 45 kcal% fat) for 16 week protected against high fat diet induced obesity by modulating adipose fatty acid synthesis and  $\beta$ -oxidation but induces hepatic fibrosis, inflammation and oxidative stress<sup>36</sup>. As hydroxy cut weight management products are widely used as weight loss supplement and number of cases is reported of hepatotoxicity. However these products contain up to 20 different ingredients, some do not contain HCA. Several case studies have been reported conducted on animal and human studies did not concluded that HCA causes hepatotoxicity. Thus it is premature to make assumptions<sup>34</sup>.

HCA have shown no observed adverse effect level (NOAEL) at levels up to 2800mg/day suggesting its safety for use<sup>37</sup>. Some weight loss supplements in which active ingredient is HCA showed potential toxicity towards spermatogenesis but it is not considered unsafe<sup>37</sup>.

### *Camellia sinensis*

*Camellia sinensis* is widely used worldwide for prevention of various chronic disorders including obesity. It is the most popular beverage across the world .it also has anti-inflammatory and immunomodulatory action<sup>38</sup>. Caffeine and catechins are active ingredients which are responsible for its activity.

The leaves of *Camellia sinensis* did not affected promptly on weight reduction. It acts by mechanism of thermo genesis and also stimulates fat oxidation, thus enhancing the metabolic rate by 4% without affecting the heart rate<sup>39</sup>. A study on human concluded that, the active component of green tea epigallocatechin-3-gallate burned more calories as compared to placebo group in



men's. Thermogenic effects also play a wide role in controlling obesity<sup>40</sup>.

The major constituent of *Camellia sinensis* is epigallocatechin 3 gallate (ECG) have a potent antioxidant and antiobesity property. It is also inhibits cancer cell growth<sup>41</sup>. It also have affect on sympathetic nervous activity by elevating energy expenditure and promoting oxidation of fat<sup>42</sup>. One study indicated that ECG have an impact on body weight gain, visceral weight, and on symptoms which is linked in promoting obesity in which high fat diet is induced in mice and examine the parameters of obesity for 16 weeks. The parameters were compared with or without treatment of ECG at a dose of 3.2 g/kg<sup>43</sup>. It also reduced the probability of hepatic steatosis and chronic inflammation in obesity. They also investigated that EGCG significantly decreased blood glucose, insulin, and insulin resistance in high-fat-fed mice<sup>44</sup>. Another study also demonstrated the highest depletion in serum cholesterol triglycerides, LDL, VLDL, HDL levels by giving orally 4ml of water extract of green tea in combination with extract of black tea and cinnamon in obese mice suffering from diabetes. The major improvement in Atherogenic Index (AI) and Coronary Risk Index in obese rats suffering from diabetes is shown in highest doses of green tea is reported<sup>45</sup>.

#### Clinical indications

*Camellia sinensis* is also beneficial in preventing other chronic diseases. It have antiinflammatory<sup>46</sup>, antioxidant<sup>47-48</sup>, anticancer<sup>49-51</sup>, neuromuscular blocking action<sup>52</sup>, immunomodulatory effect<sup>53</sup>, DNA effect<sup>54</sup>, antiviral<sup>55</sup>, antibacterial activity<sup>56</sup>, antispasmodic<sup>57</sup>, anticataract<sup>58</sup>, antigenotoxic effect<sup>59</sup>, antioxidant<sup>60</sup>, antidiabetic<sup>61</sup>, hepatoprotective<sup>62</sup>, lipid lowering activity<sup>63</sup>.

These effects are indicated by green tea by various scientists on experimental and animal models. Nowadays it is considered as most safe and healthy beverage around the world.

#### Mechanism of polyphenolic compounds in obesity

Laboratory and epidemiological studies have proved the potential effects of green tea in preventing chronic diseases. Polyphenolic compounds have briefly studied for there antiobesity action using mechanisms which inhibit de novo lipogenesis, increases lipid oxidation, increases carbohydrate utilization and decreases carbohydrate uptake<sup>64</sup>. These compounds act specifically on liver, adipose tissue, small intestine. The main active polyphenolic compound epigallocatechin 3 gallate can inhibit pancreatic lipase but the effective concentration in these studies fluctuates from 0.4  $\mu\text{mol/L}$  to 1  $\text{mmol/L}$ <sup>65-66</sup>. These catechins also metabolises the fat and regulate glucose uptake and disposition in prevention of obesity. Several studies have been reported the role of EC3G in inhibiting glucose uptake. One study has demonstrated Both EGCG and ECG have been shown to inhibit glucose transport by sodium-dependent glucose co transporter 1 (SGLT1) when the transporter was expressed in Xenopus

oocytes<sup>67</sup>. SGLT1 is expressed in intestine and EC3G is a competitive inhibitor of SGLT1. Another study have reported that green tea extract also regulate peroxisome proliferator-activated levels<sup>68</sup>.

#### Toxicity profile of *Camellia sinensis*

As it is the most popular and healthy drink, many people started consuming green tea because of its antioxidant activity recently multiple reports have been indicated liver damage by consumption of green tea were observed when administrated at high doses via concentrated extracts<sup>69</sup>.

#### Combination effect as a treatment measure

*Garcinia cambogia* and *Camellia sinensis* have proven for its efficacy for obesity and other symptoms which are interlinked with the pathogenesis of obesity. They are widely used by consumers as safe and healthy treatment for obesity. Although there mechanisms are different in lowering lipid level and fat oxidation, *Garcinia cambogia* act by two possible mechanisms, by inhibiting ATP citrate lyase, by increasing brain serotonin level which suppresses appetite<sup>70</sup>. *Camellia sinensis* act specifically on liver, adipose tissue, small intestine. It exerts its antiobesity effect in two ways lipase inhibition and thermo genesis stimulation<sup>70</sup>. Both are also available commercially in market alone or in combination. *Garcinia cambogia* and *Camellia sinensis* can be more potent and effective treatment for obesity.

#### CONCLUSION

It is evident from the above reported pharmacoepidemiological data that obesity is a matter of serious concern not only for developed countries but also for developing countries. The already available synthetic options in market like orlistat, sibutramine, rimonabant etc. These have serious side effects like hypertension, tachycardia, cognitive impairment and many more which disturbs normal physiology. Hence, it raises the utmost need of an alternative treatment like herbal drug. The herbs like *Aloe barbedensis*, *Citrus sinensis* and *Ephedra vulgaris* have been reported to have antiobesity effect. Also the other herbs like *Garcinia cambogia* and *Camellia sinensis* have the potential to treat obesity along with co morbidity. There individual as well as combined effect is of very high significance in treatment of obesity. This review paves the way for further research requires to be done at the molecular level for knowing the mechanism of action of these herbs.

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