

Health Benefits of Natural Bioactive Compound from Different Sources: Obesity

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Abstract

Obesity is a state of excessive body fat accumulation due to imbalance between energy input and energy expenditure. The worldwide disease of adiposity is seen in specific lifestyle of individuals which consume greater number of calories day by day than needed. This review of scientific literature assesses several bioactive compounds from different sources they contain that play an important role in the prevention and therapy of obesity. Bioactive compound from marines, plants, animals and dietary sources have shown anti-obesity effect. Some Prebiotics and probiotics also shown ant-obesity effects in obese individuals. Furthermore, this review focuses on various physical activities that reduces the weight gain and maintain the wellbeing of people and non-pharmacological treatments like transcranial direct current stimulation.

Keywords: Obesity, bioactive compound, visceral fat, Subcutaneous fat, Gut microbiota, Adipokines.

Background

The expanding westernization, urbanization and mechanization in most nation around the globe is related with changes in the eating routine and a sedentary lifestyle. In the past few decades people distress from 'weight gain' i.e., Obesity. Obesity is a state of excessive body fat accumulation due to imbalance between energy input and energy expenditure [1-3]. The hypothalamus, which is a part of brain control and coordinate food input and energy use, whereas muscle and fatty tissues manages food metabolism and energy generation [4]. The worldwide disease of adiposity is seen in specific lifestyle of individuals which consume greater number of calories day by day than needed [2]. Another perspective on obesity is that individuals eat close to nothing anyway they put on weight because of a moderate digestion and it isn't therapeutically upheld [5]. During obesity, numerous metabolic changes happen that can harm a few organs, for example, vascular or skeletal muscle bringing about the dysfunction of these tissues [6]. These days a few medications are being utilized for the treatment of obese patients or overweight patients. But such medicines cause various unpredicted side effects as well as have low efficacies [7,8]. So, there is a required of different to these medicines to treat obesity without or with reduced side effects [8]. Currently, diet alteration, work out, medical procedure, and Pharmacotherapy available to treat adiposity [9]. It has serious impact on human's health. Hence, it's crucial for human to find efficacious bioactive compound, functional food, drug against metabolic dysfunction [10].

Adipose Tissues

In Humans and animals, there are at least three type of fat tissues are found, which are White adipose tissues, Brown adipose tissues, and Perivascular adipose tissues (PVAT) with diverse function, anatomy and gene expression [11,12]. For the vital organs, it acts as protector and thermal controller [13]. The white fat tissue isn't just an energy supply yet in addition a secretory organ of specific molecules that have endocrine, paracrine, and autocrine activities [14]. Number of different adipokines secreted by WAT that control insulin resistance [11,12]. WAT contains macrophages, leukocytes, fibroblasts, cell ancestors, and endothelial cells. The presence of fibroblasts, macrophages, and different leukocytes, alongside adipocytes, understands the incredible assortment of proteins that are emitted by WAT under fluctuating conditions [15,16]. In people, two fundamental Storehouses of white fat tissue are separated: subcutaneous and visceral adipose tissues. Mesenteric and omental are the two kind of visceral adipose tissues [17]. In obesity, triglycerides stored in adipose tissues but ectopic fat deposition occurs mainly in liver, muscle, and heart rather than in adipose tissues [18]. Perivascular fat tissue (PVAT) is situated around the epicardial fat tissue, periaortic fat tissue [19]. BAT has been appeared to produce body heat, and react to cold and thoughtful initiation of the nervous system [20,21]. In men, Peripheral or Subcutaneous obesity is more seen, whereas Central obesity has been seen in female [22,23]. In this sense, peripheral obesity consists of accumulation of subcutaneous adipose tissues, and central obesity

comprised of accumulation of visceral fat tissues near the intra-abdominal vital organs, visceral adipose tissues has been connected with the danger of high blood pressure, hypercholesterolemia, and insulin resistance [24,25,26]. Central obesity has been demonstrated to be a significant indicator for expanded morbidity and mortality from diabetes and coronary illness [27]. Studies show that visceral fat is more firmly connected with the metabolic syndrome than subcutaneous fat [28].

Adipokines

Adipose tissues produce adipokines which have action on the immune system, metabolism and endocrine system [29]. Adipose tissues also produce proteins like leptin, adiponectin, visfatin, resistin, apelin and hormones such as angiotensin II [30,31,32]. Free fatty acid and pro-inflammatory cytokines are produced by abnormal adipocytes, which induce inflammation of tissues for examples liver, pancreas, muscle etc. [33]. In a few investigations, adiponectin level has been found decreased in individuals associated with obesity due to dysfunction of adipocytes [34,35].

Adipocyte also produced Peptide hormone leptin that helps to regulate energy balance and body weight by hindering hunger. In obesity leptin level is high in the serum due to extension of adipocytes large amount of leptin is released, and lead to chronic hyperinsulinemia [36,37]. Obesity is related with raised leptin levels. Leptin is a delicate marker for anticipating cardiovascular danger and metabolic condition [38]. Abdominal obesity has been demonstrated to be a significant indicator for expanded morbidity and mortality from diabetes and coronary illness [27]. Little known or very less levels of serum leptin detected in individuals with Congenital leptin deficiency, which is indicated by glucose intolerance, insulin resistance and severe obesity in the early age and it is because of mutation of single gene, hence known as Monogenic obesity [39]. SIM1, BDNF and NTRK2 gene mutation causes severe obesity [40]. In one investigation, the extent of bound leptin was accounted for to be higher in lean (~45%) contrasted and fat (~20%) people [41]. Obesity is strongly linked to infertility with concern to the hypothalamic-pituitary-gonadal axis and hypothalamic-pituitary-adrenal. In Obese men fertility dysfunction result by reduced testosterone levels, hinder spermatogenesis, and loss of libido (sex drive) [42].

RBP4

RBP4 is a Retinol binding protein 4 secreted by adipocyte a newly recognized adipokine has a place with the lipocalin group of protein. Expression of RBP4 occurred in mature lipid laden fat cell of adipose tissues [43,44,45]. Comorbidity of obesity like insulin resistance, type 2 diabetes is linked with RBP4, high serum RBP4 levels is unquestionably interconnected with body mass index (BMI) in both obese individuals with diabetic and without diabetic mellitus [46,47,48].

GUT Microbiota Relation with Obesity

Gut microbiota has been exhibited to assume a basic part in the event of Obesity by means of the control of energy digestion [49]. Gut microbiota also balances host immune system [50]. Studies show that gut microbiota has a close relationship with digestion through the production of metabolites inferred by intestinal microbiota, such as short chain unsaturated fats (SCFAs) that can supply colonic epithelial cells with energy [51].

Trimethylamine-N-oxide (TMAO) which is related with the arrangement of white fat tissue, and inosine-5-monophosphate (IMP) which has been discovered engaged with the digestion of lipids [49]. The connection between gut microbiota and the improvement of obesity in hosts could be because of the poisonous metabolites produced by gut microbiota, additional energy gathered from gut microbiota, and endotoxemia-related second-rate irritation [52]. For example, lipopolysaccharide (LPS), created by Gram-negative microorganisms, could cause an incendiary reaction in the host [53]. Gut microbiota includes various species, and few species such as Firmicutes, Lactobacillus, and Bacteroidetes, which is characterized as obesogenic gut microbiota, may add to the improvement of obesity [54]. Other obesogenic gut microbiota such as Rhizobium, Lactococcus, and Clostridium, are also connected with the growth of obesity [55,56].

Obesogenic gut microbiota, for example, Firmicutes, certain Bacteroidetes, Rhizobium, Lactococcus, and Clostridium, could advance the improvement of weight chiefly through the creation of SCFAs like butyrate, giving additional energy to the host, and the acceptance of poor-quality soresness brought about by the metabolites of gut microbiota [49].

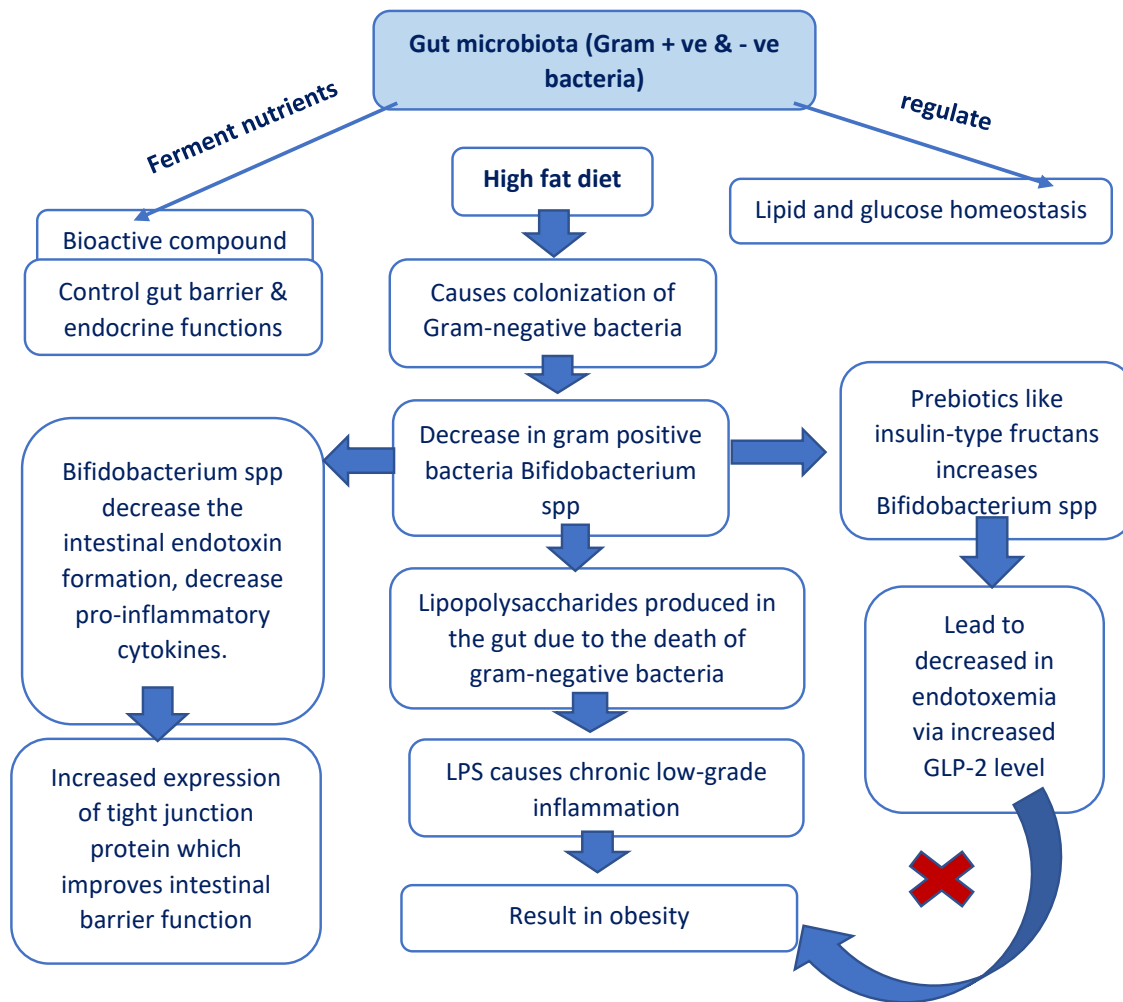


Figure 1: Disbalance of gut microbiota induced obesity

The alteration in the composition of gut microbiota promote generation of metabolic endotoxemia which lead to several metabolic disorder like obesity. Changed in microbiota may consequently change the take-up of supplements and builds energy collect. Utilizing probiotics or prebiotics in blend would be a superior procedure to forestall or lighten weight issues. In an investigation by the food organization Danisco, the probiotic strain *Bifidobacterium (B.) animalis* subsp. *lactis* 420 (B420) has been accounted for to lessen tissue inflammation and metabolic endotoxemia neutralizing the unfavorable impacts of a high-fat diet in C57BL/6 mice [57]. Human determined *Lactobacillus rhamnosus* PL60, diminished bodyweight without diminishing energy consumption and caused a critical, explicit decrease of white fat tissue in stout mice [58]. The capacity of certain probiotics such as *Lactobacillus gasseri* SBT2055 and *Bifidobacterium breve* B-3 to diminish body weight and muscle to fat ratio in corpulent patients has been demonstrated by a few clinical examinations [59,60]. Insulin-type

fructans prebiotics exhibited diminishes in the pace of adipocyte separation and the adipocyte size through overexpression of G protein coupled receptor 43 (GPR43), which is embroiled in the regulation of unsaturated fat and glucose homeostasis in fat tissue and the digestion tracts [61].

Bioactive Compounds

The innovation such as genomics, proteomics, transcriptomics, and recently metabolomics has made it conceivable to approve the utilization to conventional drugs experimentally, recognize new bioactive mixtures, clarify their systems of activity, and survey poisonousness and quality control [62]. Bioactive compounds are generally secondary metabolites, a significant number of these bioactive mixtures with various valuable activities in various body frameworks have been found from plant sources and marine and animal sources [63,64].

2. Classification of Bioactive compound

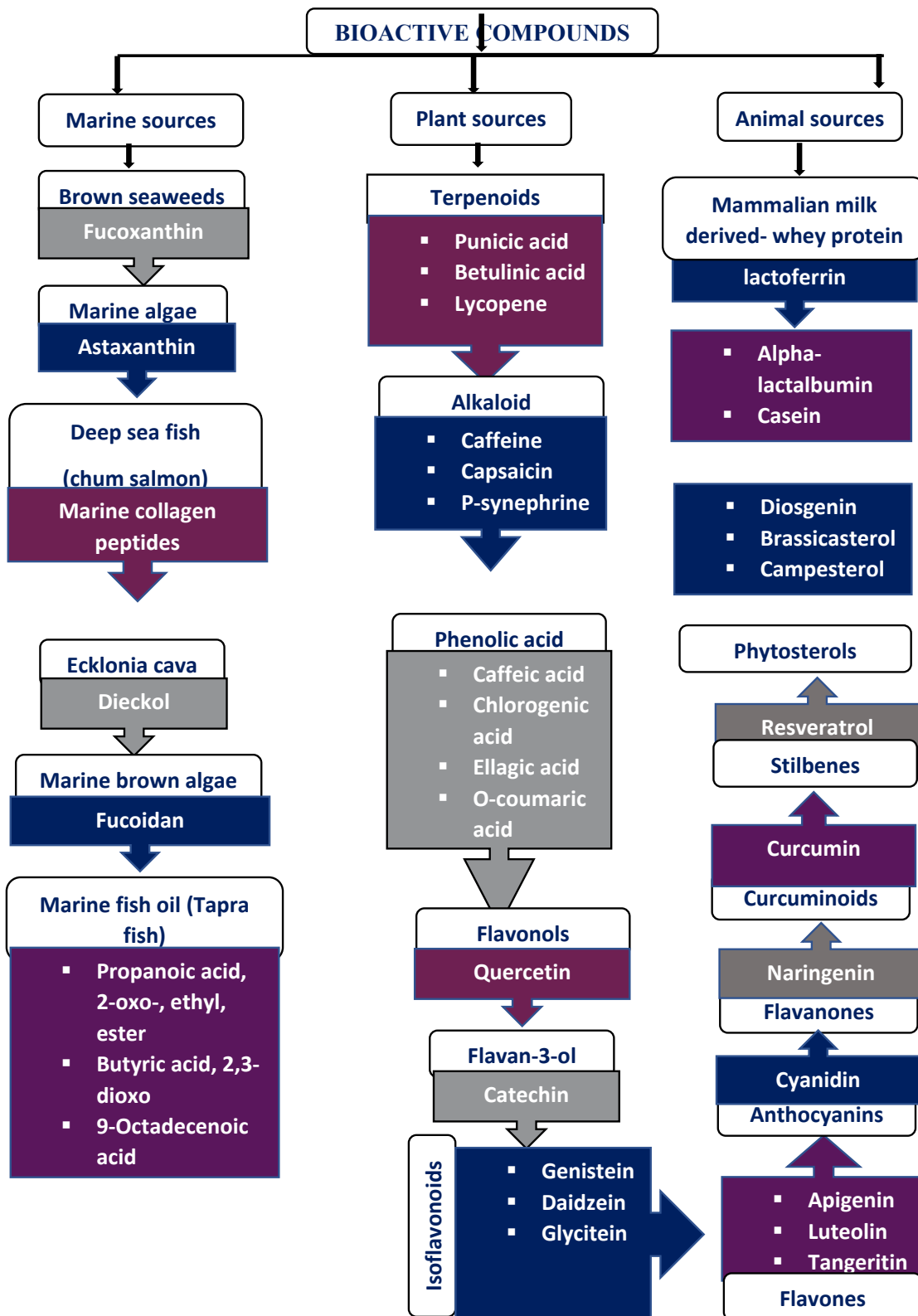


Figure 2: Classification of Natural bioactive compound

3.Pharmacological & Non-pharmacological treatment of obesity Pharmacological treatment:

Table 1: FDA approved ant-obesity drugs

Sr.no	Anti-obesity Drugs	Marketed as	Mechanism of action	Side effect	References
1	Orlistat	Alli and Xenical	Gastrointestinal lipase inhibitor (pancreatic and gastric lipase inhibitor)	Severe liver injury, diarrhea, fecal incontinence, oily spotting, bloating, flatulence, dyspepsia.	[65][66]
2	Locaserin	Belviq	5-HT _{2C} (Serotonin 2C) receptor agonist	Dizziness, depression, headache, nausea.	[65][66]
3	Phentermine/topiramate	Osymia	Norepinephrine releaser and convulsant agent	Dry mouth, paresthesia's, nasopharyngitis, birth defects.	[65][66]
4	Naltrexone/bupropion	Contrave	Noradrenaline/dopamine reuptake inhibitor and opioid receptor antagonist.	Nausea, headache, insomnia, constipation.	[65][66]
5	Liraglutide	Saxenda	Glucagon-like peptide-1 agonist (GLP-1)	Nausea, vomiting, diarrhea, constipation, dyspepsia.	[67]

Ref: Sun NN, Wu TY, Chau CF. Natural dietary and herbal products in anti-obesity treatment. *Molecules*. 2016 Oct;21(10):1351 [65].

Ref: Kang JG, Park CY. Anti-obesity drugs: a review about their effects and safety. *Diabetes & metabolism journal*. 2012 Feb;36(1):13 [66].

Ref for liraglutide: Tak YJ, Lee SY. Long-term efficacy and safety of anti-obesity treatment: where do we stand? *Current Obesity Reports*. 2021 Jan 6:1-7 [67].

Table 2: Current advanced in the Pharmacological treatment against weight gain

Sr.no	Target	Target location	Drug	Mechanism of action	Side effects
1	Cannabinoid-1 (CB1) receptor (G-protein couple receptor)	Hypothalamic nuclei	Rimonabant	CB1 receptor inhibitor	Change in mood, anxiety and depression
2	β3 – adrenoreceptors (G-protein couple receptor)	Brown adipose tissues (BAT)	Mirabegron and Solabegron	Increased lipolysis & free fatty acid mobilization in WAT and thermogenesis in BAT through increase in adenylyl cyclase and increase in cAMP production.	NA
3	Melanocortin receptors 4 (MC4R)	Brain (CNS)	Setmelanotide	Melanocortin receptor 4 agonists (MC4R)	Skin cancer development and darkening of skin pigmentation & hair colour

Ref: Schellack N, Grobbelaar S, Wadesango L, Bronkhorst E, Kupa K. New advances in the management of obesity. *SA Pharmaceutical Journal*. 2021 Jan 1;88(1):17-21. [68]

Non-pharmacological treatment:

1) Various bioactive compound used in management and treatment of obesity from natural materials.

Table 3: Various bioactive compound from natural sources

Sr.no	Source	Bioactive constituents
Fruits		
1.	Apples	Procyanidin, quercetin
2.	Mulberries	Anthocyanin, quercetin, chlorogenic acids
3.	Strawberry	Anthocyanin
4.	Blueberries	Hydroxycinnamic acid, resveratrol
5.	Grapes	Proanthocyanidins, resveratrol (skin of red grapes).
6.	Pomegranates	Resveratrol
7.	Banana (pulp and peel)	Gallic acid, catechin, anthocyanin,
8.	Citrus peel	Polymethoxyflavones and hydroxyl polymethoxyflavones
Vegetables		
1.	Broccoli	Thylakoid
2.	Onion	Quercetin
Spices		
1.	Ginger	Gingerols
2.	Turmeric	Curcumin
3.	Chili	Capsaicin
4.	Cinnamon	Cinnamon oil
5.	Garlic	Allicin
6.	Rosemary	Carnosic acid
Legumes		
1.	Mung bean	8-globulin
2.	Soya beans	Genistein

Dietary Calcium

A few researchers have detailed that a high intake of dietary calcium may reduce the adiposity due to increase fecal fat discharge and energy use [69]. The mechanism of expanding fecal fat discharge is most likely because of the arrangement of insoluble calcium-unsaturated fat cleansers as well as restricting of bile acids [70]. Also, high dietary calcium (Ca²⁺) has been accounted for to have against anti-inflammatory properties [71].

Dietary Fiberz

Soluble dietary fiber like pectin's, gums, hemicellulose, mucilage and β -glucans and insoluble dietary fiber like cellulose and lignin are used as anti-obesity agent. Dietary fiber could behave like a physiologic impediment to bring down energy consumption [72]. From epidemiological investigations, it is notable that dietary fiber consumption, particularly consumption of entire grains or oat fiber, secure against advancement of stoutness [73,74]. Viscosity and fermentability are the two physicochemical properties that have been perceived as creating gainful physiological impacts [75]. Viscosity of soluble dietary fiber increase into the small intestine due to the liquid, which may introduce an obstruction to moderate gastric exhausting and postpone supplement retention [76]. Fermentable DFs are more viable at advancing discharge of GLP-1, one of the primary anorexigenic peptides [77].

PUFA

Dietary intake of Tapra fish may reduce the obesity due to the tapra fish oil, which contained omega-3s polyunsaturated fatty acids (n-3 PUFA) such as Eicosapentaenoic acid, Docosahexaenoic acid, Propanoic acid, 2-oxo-, ethyl, ester, Butyric acid, 2,3-dioxo and 9-Octadecenoic acid [78]. PUFA action is basically because of changes in gene expression levels of enzymes in the liver, specifically a diminished mRNA expression of Fatty acid synthase, stearyl-CoA desaturase-1 and acetyl-CoA carboxylase alpha, which are liable for lipid synthesis [79,80]. In this way, they may keep away from free unsaturated fats entering adipocytes for lipogenesis and additionally improve lipid oxidation and thermogenesis [81].

Protein

Numerous high proteins daily diet from animals and plants sources reported to reduces obesity by different mechanism. Whey protein isolated from mammalian milk shown production of various bioactive peptides by its gastrointestinal processing [82,83]. Which inhibit the food intake and expanded satiety via release of anorexigenic cholecystokinin, peptide YY and reduced the release of ghrelin hormones into the digestive tract [84].

Consumption of lactoferrin, whey protein has as of late been ac-

counted for to diminish abdominal obesity, whereas persistent consumption of lactoferrin has appeared to diminish visceral obesity in people [85,86]. Another significant milk-determined whey protein is Alpha lactalbumin, which has shown hunger suppressant effects and casein whey protein derived hydrolysates has shown satiety effect by potential mechanism via secretion of gut hormones such as cholecystokinin and GLP-1 [87,88].

2) Regular Physical Exercise

Expanded physical exercise can be utilized to adjust energy consumption by expanding the amount of energy a body employment. Regular physical exercise like walking, running, skipping, are beneficial in the maintenance of disbalance in energy intake and energy expenditure. The general objective of physical activity in the treatment or avoidance of weight gain is weight reduction. To move toward this objective, the Institute of Medicine of The National Academies of Science distributed the suggestion to embrace 1 hour of moderate physical activity a day all week long with no difference in caloric admission [89]. The actual advantages of a regular exercise in fat patients are predominantly portrayed in an alteration in the metabolism, for example, an improved liver capacity and chemical capacities, similar to an expanded insulin and leptin affectability just as expanded ghrelin levels [90,91,92,93]. The American College of Sports Medicine suggest ceaseless or irregular aerobic exercise at a recurrence of three to five times each week, however minimum 150 min of aerobic activity (e.g., brisk Walking or cycling) each week to create and keep a sound way of life [94,95]. Daily aerobic exercises are related with various advantages remembering enhancements for physical and psychological well-being [96]. Physical activity also is associated with improved fitness, which may attenuate the risk of mortality associated with obesity. Regular physical exercise additionally is related with improved wellness, which may weaken the danger of mortality related with weight gain [97].

3) Transcranial direct current stimulation

The capacity to control food craving is related with chief working, which begin in the prefrontal cortex (PFC) [98]. Research in the prefrontal cortex (PFC) of encephalon area of obese individuals demonstrates a strange action in the left dorsolateral Prefrontal cortex (DLPC) associated with obesogenic behavioral regulation and flavor. It was seemed to have left dorsolateral Prefrontal cortex (PFC) less activation in obese individuals and those liable to eat too much [99]. Expanding DLPFC movement may improve the capacity to control food craving, giving a novel worldview in the treatment of stoutness [100]. Transcranial direct current stimulation (TDCS) approaches are important to advance behavioural changes, prompting effective weight reduction. This procedure is a non-invasive which include the use of 2mA constant electrical current over the scalp [101]. The current is produced from a battery-controlled gadget, where it is conveyed to the cerebrum through an anode terminal and gets back to the gadget through a cathode terminal [102,103]. the specific mechanism of TDCS is not completely perceived, it seems the current represses synapses at the neural connection; the anode is related with the hindrance of

gamma-aminobutyric acid (GABA) though the cathode is related with the restraint of glutamate [102,104].

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Conclusion

It is adequate that exorbitant energy consumption that surpasses energy use is one of the primary drivers of weight. Different pharmacological and Non-pharmacological procedures have been created intended to oversee and forestall this medical problem. The utilization of bioactive compound is potential option for treatment and management of weight gain. Non-pharmacological treatment systems for the improvement of viable and safe enemy of anti-weight gain drugs items, could be considered as a steady instrument to keep corpulent individuals hanging on their weight reduction objectives. Bioactive compound from various sources such as plants (Fruit & vegetable), animal and marine sources being of biological origin have little side effects in comparison to current pharmacological drugs, which were approved by the FDA. Bioactive compounds may give against weight gain impact as well as other medical advantages, for example, hostile to diabetic and hostile to hyper-lipidemic exercises. All in all, further exploration should go toward bioactive compound from various sources to show new preventive and possible helpful techniques against metabolic disease.

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