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Review Article

Examination of the Obesogenic Effects of Bisphenol-A

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ABSTRACT

The prevalence of obesity among people has increased dramatically in recent years in all the world. It is not enough to explain this increasing trend only with people's lifestyle, eating habits and cultural differences. Some chemicals, which are taken into the human body, especially through the food chain and are considered to be endocrine disruptors, affect the frequency of obesity. Endocrine disrupting chemicals (EDCs) are compounds that cause hormone disruption and elimination of the functions of these hormones. Bisphenol-A (BPA) is one of the most intensive chemicals in human life and is generally called 2,2-bis (4-hydroxyphenyl) propane. 70% of the BPA in the world is used in polycarbonate plastics and 30% in epoxy resins. Due to the widespread usage of it, BPA reaches solid and liquid wastes in terrestrial and aquatic ecosystems in large quantities. Considering the high production capacity of BPA and its different application areas, it is claimed that significant amount of BPA enters the environment. Studies show that the rate of being exposed to BPA has an increasing tendency. In the literature, the rate of availability in drinking water and the data on the reproductive system were only included in the researches related to BPA. Therefore, this study aimed to observe the obesogenic role of BPA in the development of obesity, which is the current health problem of the world. BPA is an endocrine disrupting chemical known to have in vitro effects on glucose metabolism and adipose tissue. In a limited number of clinical and epidemiological studies, BPA has been shown to be associated with diabetes and obesity. For this purpose, the current literature related to this issue has been reviewed and the effects of BPA on obesity have been compiled both in the world and in our country.

1. Introduction

Nowadays, obesity is accepted as an important issue that is called as a widespread worldwide problem by the international standards and it is a persistent illness that needs treatment. Obesity prevalence has increased markedly over the past few decades. The worldwide prevalence of obesity is increasing at an alarming rate. Cumulative evidence offers that ecological components, especially hormonal disorder compounds, may also have a role in the rise of obesity (see Figure 1) [1, 2]. Obesity is a problem for all ages, and the number of children and youths who are overweight has risen in parallel with the rates reported in adults [3]. With important social and mental responses, obesity is a sophisticated illness affecting nearly all ages, genders, and ethnic groups. Moreover, obesity and excess weight are major contributors to the international load of chronic illness and are link to type 2 diabetes, heart disease, gout, liver disease, kidney disease, and some forms of cancer [3]. Childhood obesity has become one of the most important health issues of the last 10 years. Obesity can affect a kid's body health through cardiovascular, hormone, psychosocial situation, irregular eating habits, and depression [1, 2]. Obesity can also effect success at school. In addition to sanitary effects, childhood obesity has also economical conclusions [3, 4] (Figure 2). In OECD countries, according to Body Mass Index (BMI) values, the obesity rate ranged from 15% (Norway) to 45% (Chile). In addition, the obesity level in different age groups is identified as 26% on average in males and 24% in females. The prevalence of overweight women is higher than men in some countries (Figure 3).

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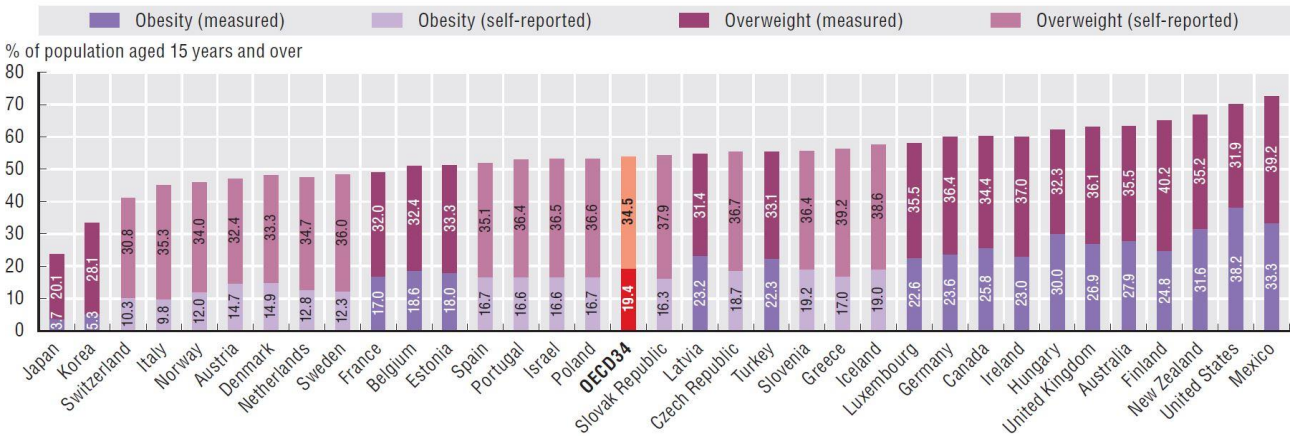

Figure 2: Obesity rates for OECD countries in 2015 or nearest year [2, 105].

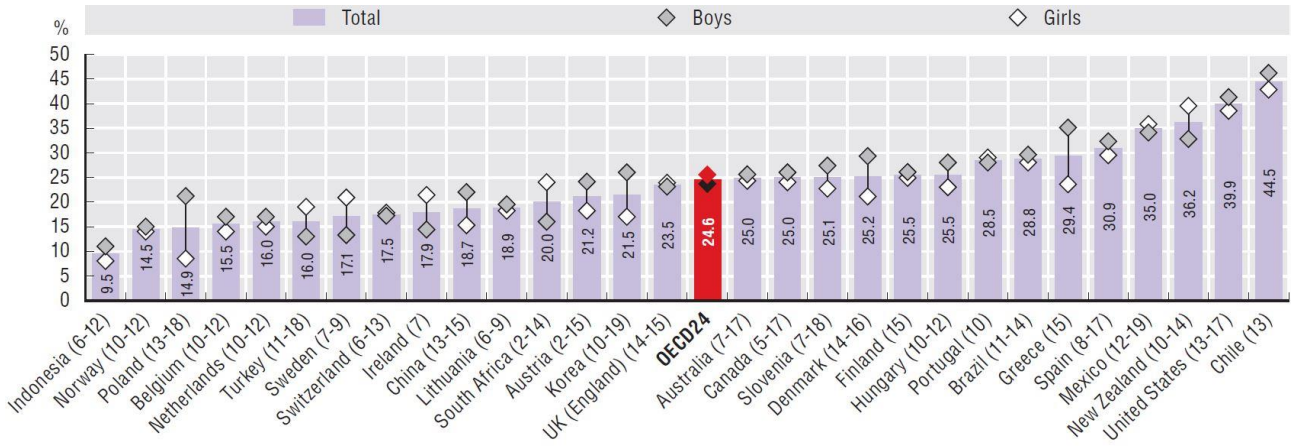

Figure 3: In some countries between the ages of 6 and 19, the distribution of obesity among children in the last 5 years [2, 105].

Nowadays, a lot of contaminants called as endocrine-disrupting (diethylstilbestrol, persistent organic pollutants, Bisphenol A, phthalates, polybrominated biphenyls, 4-Nonylphenol, parabens, phytoestrogens) is indicated to break the activities of hormones. Also, such chemicals are termed as “obesogens”. These chemicals themselves and their by-products are heavily involved in nature as a result of human activities. Throughout their daily lives, human beings are now exposed to this obesogens in external and internal habitats through their usage of pesticides, industrial and domestic products, plastics, cleaners, cosmetics. The input of them to the living system may be through oral, respiration or dermal suction [4-6]. From farm to fork, our food carries thousands of obesogens that we consume. Obesogens cause weight increase by changing fat homeostasis to promote the fat collection, and this may occur through the complex systems summarized in Figure 4 [2]. With their different hormone-like activities, endocrine-disrupting contaminants, which can be classified into persistent and non-persistent groups depending on their biodegradation and bioaccumulation properties, have diverse effect on the endocrine systems. [7].

BPA (2,2’-bis-4-hydroxyphenyl-propane) is an endocrine-disrupting chemical produced in large quantities worldwide [8]. BPA, which was first produced in the 1940s as an artificial estrogen, is used for its diagonal-structure features in the production of carboy materials, which are immanent in user products such as plastic materials, platings on food, thermic paper [9]. 2,2’-bis-4-hydroxyphenyl-propane is one of the World’s maximum generation capacity obesogens [10-14]. At the present time in the science world, the harmful effect of a phenolic type of ecological toxic substances, known as BPA, has attracted the major attention [15].

Table 1. BPA concentrations in the major sources [17].

Affected Sources	BPA Concentration	Units
Aquatic media	8000-21000	ng/L
Air	0.002-0.208	ng/L
Dust	800-10000	ng/g
Thermal paper	54000-79000	ng/cm^2
Fish	5-109	ng/g
Foods	9-76	ng/g
Cosmetics	21-43	ng/g
Cans	2-82	ng/g
Plastics	0.2-26	ng/g
Dental materials	13000-30000	ng

Suitable sources of possible exposure to BPA in habitats are shown in Table 1 [16, 17]. Since BPA is classified as an obesogen related to some disease in cell and animal models, apprehension has increased for community health [10]. Several epidemiological studies have also found results on the associations of BPA levels with some diseases such as type 2 diabetes, heart illness, obesity and sexual disorders [13]. In this study, the aim of the literature search was to find all studies examining the relationship between BPA exposure and human health or physiological changes in humans.

2. Material and Methods

With no time or language limitations, all academic fields focusing on the environmental obesogens were detected by using MEDLINE, PubMed, Google Scholar, ISIWeb of Science, Springer, Taylor-Francis, Elsevier, and Scopus. The scientific studies were monitored during May, June, July and August 2017. Searching process in all the databases was conducted through using the different keywords (endocrine disruptors and chemicals, obesogen, BPA, BPA and obesity, obesity and overweight, excess weight, body mass index, weight gain, childhood obesity, etc.).

3. Literature Survey and Discussion

2,2'-bis-4-hydroxyphenyl-propane is an obesogen of synthetic polymer used in all packing and in epoxy resins used as coverings in nutrient boxes. With the biological monitoring system applied today, BPA monitoring can be performed in urine and blood samples of 93% of the people. [18]. Scholars have determined BPA in the blood of mature women, in navel cord liquid and in placenta [19, 20]. In the experimental studies with laboratory animals, it was found that BPA affected the reproductive system negatively [21]. In all studies conducted to identify BPA, it was observed that especially in the childhood period, the hormone system collapsed and cancer types became prevalent [22-25]. In both male and female, higher BPA levels in urine were associated with different diseases (diabetes, obesity etc.) [26-30]. In some studies, on all living beings, there was an expanding proof related to BPA's obesogenic impacts. It was found that perinatal and postnatal exposure to BPA in aquatic solution was related to increase in heaviness and whole cholesterol in lab mouse [31-41]. Some literature review was conducted to find all studies examining the association between BPA exposure and childhood obesity [42-47]. In the academic field, some research has tried to explain the technics of mutual effect of BPA and hormones. Especially, in-vitro and in-vivo studies have supported the theory of exposure to BPA [49-51]. In recent years, it has been determined that BPA content materials used intensively in childhood increase obesity and diabetes. [52-54]. Table 2 presents the major medical studies that examined the relationships between BPA and early-age obesity. Certain scientific research recorded the link of the exposure to some obesogens with obesity. BPA is one of the obesogens described by the experimental studies [55-61]. Previous studies have supported the link between obesity and low dose exposure to endocrine disrupting chemical such as BPA, which are commonly found in plastics, dental equipment, food, beverage cans [62, 63]. Summarizing the effects of obesogens, because of their lipophilic structure, they increase the rate of fat retention in living beings [64].

There is no study examining the obesogenic effects of BPA in our country. Recently, the prevalence of obesity and childhood obesity has been examined in Turkey. Childhood obesity is a major issue in Turkey (Table 3). In a study conducted in Istanbul on children between 1-11 years old, it was indicated that 36.1% of the children were fat or obese [65]. It has been noticed in the other studies that some of the parameters of obesity-causes in the childhood period are heritage, gender, ethnicity, eating habits, amount of nourishment between 0-1 years, and insufficient physical activities [66, 67]. The aim of the study in the Çorum was to define the results in terms of being overweight or obese for children from 3 to 6 years old and to guide the children and their parents in making healthy nutrition selections by informing them. Findings of the research indicated that 26% of the test subjects who joined in the study were fat or obese [66]. In national and international studies, it has been notified that boys are more obese in comparison to girls [68]. Other studies conducted in these regions have shown a more obesity rate in men than in women. Obesity is more extensive among men in Turkey because we have a male dominated society and thus more attention is given to boys' nourishment [66, 69-73]. In another study, Şenyıldız et al. [74] examined the effects of BPA on gene evidences, histone changes and endocrine disrupting chronic toxicity in the population. The potential health impacts of BPA on urinary system, including the seminal mechanism, and pubertal improving was discussed by depending on some of the available literature [75-83]. Balcı et al. [79] investigated the mutual effect of phthalates and BPA with both adipogenesis and obesity by promotion in artificial environment, animal and human results. In the available research, Topçu et al. [78] intended to consider effects of the psychologic status in fat children.

The results, inclusive in this short compilation, support a hormone system connection between the exposure to EDCs and the increasing of obesity. The obesogenic effects of EDCs are not only caused by chemicals. At the same time, people's genetic structures, eating habits and lifestyle also affect obesity. In Turkey, use of BPA was banned in baby bottles, and other polycarbonate baby

products in July 2012 by a regulation which was included in the Turkish Food Codex-baby formulas [84-87]. However, there are still cheap baby bottles, toys, or baby care products containing BPA in the market. On the other hand, in worldwide and Turkey, there is a tendency to consume easily made, tinned, or packaged food instead of home-made nutrition among children and adults. As the number of working women rise, it is inevitable that nutrition of boys and girls will be fast-food or microwave-meal.

3. Conclusions

The studies in the literature show that exposure of everybody to obesogens will cause excess weight and obesity. The number of research related to obesogens and especially the effect of BPA on children, is increasing day by day. However, because of the higher sensitivity of child to peripheral compounds exposures and for specifying systems of the obesogenic impacts of BPA, extra studies are required to investigate the relationship between BPA response and childhood health results. Several countries have issued regulations to ban the usage of BPA in specific products, such as baby bottles. Similar applications should be proceed to modify BPA with different plastic materials and to decrease the influences of these components.

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Table 2. Abstract of investigations evaluative the relationship between BPA and different illness.

Disease Type	Study population (person)	Population type	BPA Amount (ng/ml)	References
Diabetes	3516	Adults (≥40 aged)	1.43-2.22	[44]
Obesity	1455	Adults (≥40 aged)	4.5-4.7	[48]
Diabetes/Obesity	296	Female	1.38	[49]
Type 2 diabetes	3423	Adults (≥40 aged)	0.8-2.1	[50, 51]
Obesity	76	Male	1.04	[52]
cardiovascular diseases	596	Male/Female	1.3-1.5	[53]
cardiovascular diseases	1619	Adults (≥30 aged)	1.2-1.4	[54]
Obesity	977	Adults (≥40 aged)	0.8-5.0	[55]
Obesity	2747	Teenagers (≥18 aged)	2.1	[56]
Obesity	890	Adults (≥70 aged)	2.1-3.9	[57]
Obesity/ Type 2 diabetes	3390	Adults (≥40 aged)	0.8	[58]
Obesity	223	Teenagers (≥18 aged)	2.85	[59]
Sex Hormones	282	Female	2.3	[60]
Obesity	3967	Teenagers (≥20 aged)	3.9-4.0	[37].
Obesity	85	Female	1.5-1.7	[61]
Obesity	82	Male/Female	1.3	[62]
Obesity	1521	Adults (≥40 aged)	0.6-2.6	[63]
Obesity	2200	Teenagers (6-18 aged)	15.-5.4	[64]

Table 3. Selected studies on overweight/obesity prevalence among children and adults in Turkey.

Previous Studies	Year	Regions	Age ranges	Obesity (%)	Overweight (%)
[88]	2001	İstanbul	3-18	4.3	17.6
[89]	2002-2003	Antalya	6-17	3.6	14.3
[90]	2004	Ankara	10-16	3.6	10.7
[91]	2004	Kayseri	6-17	1.6	10.6
[92]	2005	Aydın	6-16	3.7	12.2
[93]	2007	Elazığ	6-11	1.6	13.2
[94]	2008	Bursa	6-12	10	12.4
[95]	2008	Bolu	6-17	6.1	10.3
[96]	2009	İzmir	2-15	6.3	9.9
[97]	2009	Kocaeli	10-19	6.8	11.5
[98]	2009	Samsun	11-14	10.3	22.4
[99]	2009-2010	Kayseri	0-7	4.9	10
[100]	2010	Van	6-18	2.2	11.1
[101]	2010-2011	Ankara	11-18	7.7	11.1
[102]	2011	Mardin	6-15	10.6	15.8
[66]	2016	Çorum	3-6	12.1	14.3
[103]	2008	Tokat	≥18	29.5	30
[104]	2007-2009	İzmir	≥30	39.1	37.4

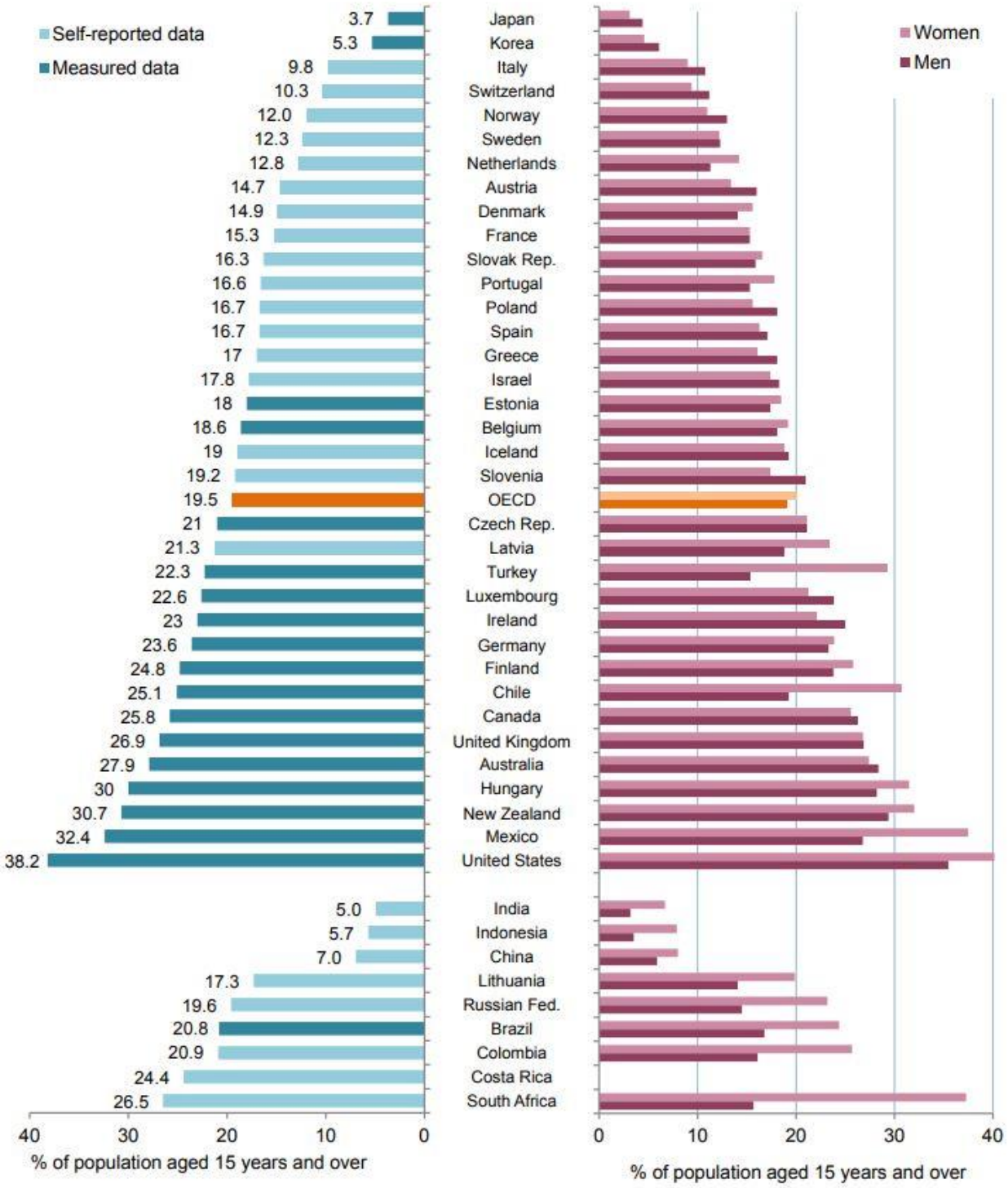

Figure 1: Obesity among adults, 2015 or nearest year, OECD Health Statistics 2017 [105].

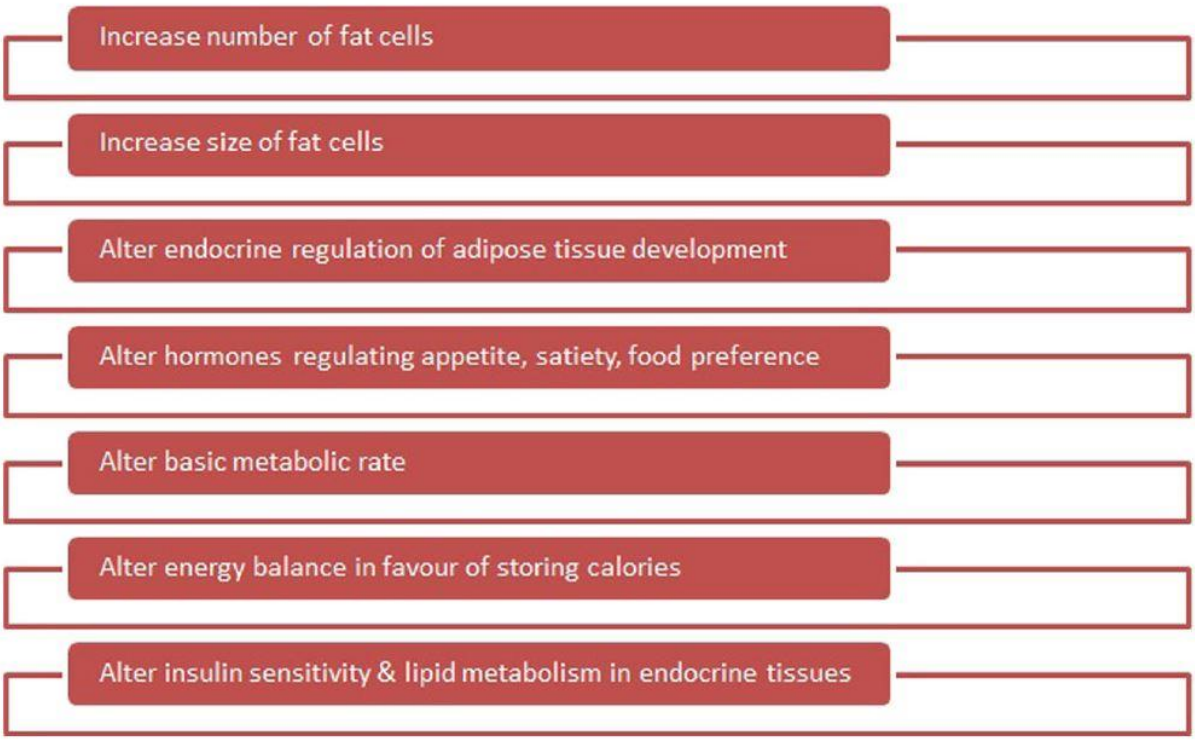

Figure 4: Summary of the mechanisms of obesogens [2].