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Sugar and cardiovascular diseases

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Abstract

Cardiovascular diseases are the leading cause of death in the Spanish population and may be a relationship between the prevalence of these and excessive sugar consumption. In recent years, researchers have focused on the properties of these nutrients. Although there are many studies examining this association, the results are not unanimous. In any case there is sufficient basis for designing public health strategies in order to reduce the consumption of sugary drinks as part of a healthy lifestyle.

Therefore, the question we address is: sugar intake in abundant amounts, is associated with a higher risk of cardiovascular disease? We use as the focus of the discussion SAFO analysis model.

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Key words: *Cardiovascular diseases. Sugar consumption. Sugary drinks.Healthy lifestyle.*

AZÚCAR Y ENFERMEDADES CARDIOVASCULARES

Resumen

Las enfermedades cardiovasculares constituyen la principal causa de muerte en la población española y podría existir una relación entre la prevalencia de las mismas y el consumo excesivo de azúcar. En estos últimos años, los investigadores se han centrado en las propiedades de estos nutrientes. Aunque existen muchos estudios que analizan dicha asociación, los resultados no son unánimes. En cualquier caso, existe fundamento suficiente para diseñar estrategias de salud pública de cara a reducir el consumo de bebidas azucaradas, como parte de un estilo de vida saludable.

Por lo tanto, la cuestión que abordamos es: ¿la ingesta de azúcar, en cuantía abundante, se asocia un mayor riesgo de padecer enfermedad cardiovascular? Para ello utilizamos como eje de la discusión el modelo de análisis DAFO.

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Palabras clave: *Enfermedades cardiovasculares. Consumo de azúcar. Bebidas azucaradas. Estilo de vida saludable.*

Abbreviations

AMP: Adenosine monophosphate.
HBP: High blood pressure.
BMI: Body mass index.
MAPA: Arterial blood pressure monitoring.
WHO: World Health Organisation.

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Introduction

The term sugar or sugars tends to be used to designate the different monosaccharides and or disaccharides which are characterised by having a sweet taste, but by extension its is used to make reference to practically all carbohydrates. 70% of the world's sugar is produced from sugar cane and the rest from beet. We know of the existence of sugar cane thanks to one of Alexander the Great's Admirals (356-323 b.c) named Nearco who mentions it in an expedition to India. From Roman times there are references towards elaborated sugar; for example, in the chronicles of the storming of the King of Persia's Palace by Emperor Flavio Heraclio Augusto's (575-641a.d.) troops in 627 a.d. sugar was part of the bounty, along with silks and varied spices. Nowadays, sugar is consumed by the majority of the population and is

widely appreciated for its ability to make food more appetising[1].

During recent decades, the physiological properties of carbohydrates and sugars have not drawn excessive interest from the scientific community, who concentrated more on saturated fats, which until recently dominated the nutritional panorama. In recent years, however, researchers have concentrated on the properties of sugar, and in particular in fructose. This monosaccharide forms part (along with glucose) of sucrose, a disaccharide more commonly known as "table sugar". Sucrose (fructose and glucose) is added to a large number of manufactured foods (yogurt, cereals, sauces, cakes, biscuits) and drinks (tea, coffee, soft drinks)[2].

In this chapter we analyse the relationship between sugar (glucose and fructose) and cardiovascular disease, to answer the following question: is the consumption of sugar, in large quantities, associated with a higher risk of suffering from a cardiovascular disease?

Current state of the problem

Cardiovascular disease is the main cause of death in the Spanish population. In our country the prevalence of the main cardiovascular risk factors is high[3-4]. In the ERICE5 study (the aggregation of eight cross-sectional epidemiological studies, carried out in Spain between 1992 and 2001) the most common cardiovascular risk factors were high cholesterol (46,7%), high blood pressure (37,6%), tobacco consumption (32,2%), obesity (22,8%) y diabetesmellitus (6,2%). This prevalence of diabetes mellitus is in contrast to that obtained by the MAPA Group in the city of Madrid (10,6%)[4] and with the most recent figure by Soriguer et al6 in Spain (13,8%; CI 95%, 12,8% a 14,7%), of which half did not know they suffered from diabetes (6,0% [CI 95%, 5,4% a 6,7%].

The inhabitants of developed countries now consume more calories than in yesteryear. Obesity, defined as an excess of body fat, is the result of a positive energy balance, and is the most frequent form of malnutrition. The calorie consumption has increased on average from 150 to 300 calories per day. Almost 50% of this increase comes from liquid calories, in particular sugary drinks, manufactured in the main with fructose. The consumption of fructose is considered to contribute to the higher obesity rate in industrialised countries, as there is a temporary relationship, parallel and direct between their consumption and the increase in obesity. In some sections of the population of the United States, the intake of these drinks accounts for 15% of the daily-recommended calorie intake.

Alternatively, sugar is an essential ingredient in our diet. It provides a rapid and important energy source. It is part of oral hydration, so relevant for people who practice sport. It can help the sick and elderly who have a lack of appetite to consume nutritionally desirable foods. Sugar and salt are great natural preservatives, which, during centuries and until the discovery of industrial cold preservation (fridges) were the only preservatives available[1]. Furthermore, a very important aspect, related with the festive or emotional facet is the pleasure that it brings. We cannot envisage a party without a cake, a Christmas without nougat (*Turrones*) or a wedding without a cake.

However, it seems to be necessary to reflect upon the epidemic proportions that obesity is reaching, with the objective of establishing the most adequate therapeutic strategies and in this context, analyse the role of certain foods, as is the case of sugary drinks, as well as the evidence available to enable us to offer messages to the general public regarding moderation and restriction of their consumption.

So why is the intake of sugar, above the recommended quantities, (OMS: 10% of the total calories in the diet in the form of sugars), associated with a higher risk of suffering from a cardiovascular disease? This is the subject analysed in this chapter (Table I).

Strengths

In the last 25 years excess weight and obesity has increased notably, in relation to a positive energy balance, which is related to a clear drop in physical activity (especially notable in Spain) and with a less balanced diet with a lowering of carbohydrates and increase in fat consumed, with a total calorie intake lower to that of previous years.

The very high consumption of fructose, higher than current consumption levels, has been associated with an increase in the levels of triglycerides, visceral fat, blood pressure, resistance to the hypoglycaemic action of insulin and a drop in the levels of HDL-cholesterol. These variations taken alone or as a group have been associated with the increase in risk of suffering from some type of cardiovascular disease[7]. A large part of these effects of fructose is due to the fact that nearly 50% of the quantity absorbed is converted into fatty acids, as opposed to other carbohydrates, such as starch, which only 5% is converted into fatty acids.

Its excessive consumption has also been associated with high levels of urate serum. Fructose is converted in the liver into fructose-1 phosphate. The phosphorylation of the fructose also carries an increase of the synthesis of AMP, part of which can enter the degradation path of the purine nucleotides, which culminate in the synthesis of uric acid (Fig. 1). Diverse epidemiological studies have shown a significant relationship between uraemia and the appearance of a cardiovascular disease, high blood pressure (HBP), diabetes and a resistance to the hypoglycaemic action of insulin.The rise of uric acid levels in blood has been associated

Table I

SWOT Analysis (Strengths, Weaknesses, Opportunities and Threats) overall application: the intake of sugar, in large quantities, is associated with a higher risk of suffering from cardiovascular disease

Strengths	*Weaknesses*
Inherent elements (internal) in the binomial sugar and cardiovascular disease that strengthen this relationship: • Possible deleterious effects of sugar: – Obesity[3]. – Reduction of HDL[9]. – Hyperuricemia[11]. • Increase in birth weight[38].	Inherent elements in the binomial sugar and cardiovascular disease that weaken this relationship: • CARMEN Study[22]. • The reduction of fat and slight increase in carbohydrates associated with weight loss[24]. • Australian paradox[25].
Threats	*Opportunities*
External elements for binomial sugar and cardiovascular disease that "threaten" this relationship: • The genetic influence in the development of obesity[26]. • The excessive consumption of fats associated with obesity[27]. • Role of intestinal microbiota in obesity[30]. • Being sedentary also influences obesity[31].	External elements for binomial sugar and cardiovascular disease that offer the possibility to demonstrate a direct scientific relationship: • Promoting education of healthy dietary habits (with the family, at school, healthcare professionals)[24].

independently, with the cardiovascular related morbidity, even though not all the epidemiological studies offer concurring results. In patients with HBP and diabetes this association is more intense than in the general population. It is estimated that in comparison with individuals with normal serum urate levels, patients with hyperuricemia have a medium risk of suffering ischemic cardio pathology or essential HBP 10 times higher. This pathological association can be explained by the endothelial dysfunction. The hyperuricemia cannot only be the cause of the endothelial damage, but a consequence of it. The hyperuricemia can be explained by an excessive production of urate caused by a higher influx of AMP (Fig. 1). But also, the increase in serum urate can be a consequence of a drop in its renal secretion related to the resistance to the hypoglycaemic effect of the insulin and/or the deterioration of renal function (nefroangioesclerosis). For some authors the sex of the subject can influence in the relationship between hyperuricemia and HBP, with a significant association, more intense in men than in women.

It is important to point out that a lot of literature regarding the consumption of high calorie drinks originating in North America, without the possibility of differentiating the results obtained relative to drinks sweetened with sugar to those that contain other sweeteners (such as high fructose corn syrup).

Recently three studies have been published that show the influence of sugary drinks (rich in fructose) on the development of obesity in children, teenagers and adults[8-10] (Table II). These three studies formulate a common conclusion: excessive ingestion calories are possibly responsible.

Some studies have related the consumption of sugary drinks during pregnancy with the increased weight of the baby when born. The temporary parallel tendency estimates that based on commercial sales figures, between the consumption of sucrose, in the country where the study took place (Norway), and the higher percentage of overweight babies, supports this hypothesis[11].

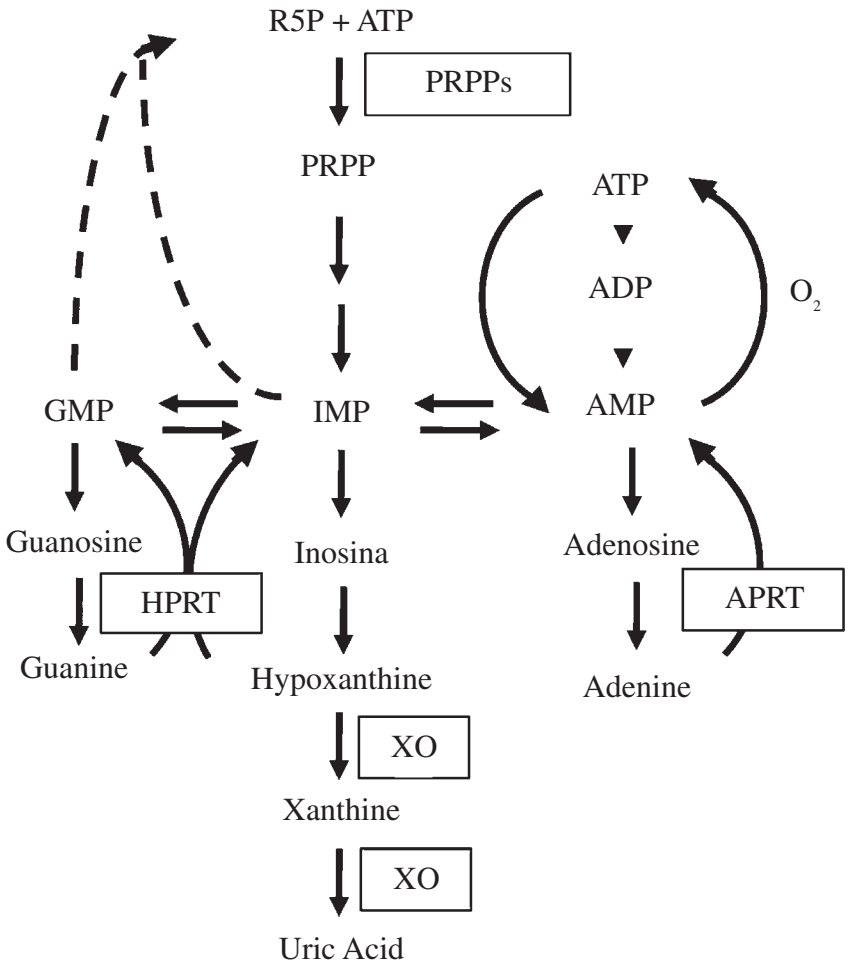
When examining the complete scientific evidence, which exists today, it does not allow us to demonstrate convincingly that the effects attributed to sugary drinks are exclusively due to those sugary drinks but can be associated with any high calorie drink[12].

Weaknesses

The claim that the intake of sugar, in large quantities and in all cases way above the current level of consumption, is associated with a higher risk of suffering a cardiovascular disease shows weaknesses; not all studies support this claim. This can be seen in the CARMEN[13] report where fat was substituted by carbohydrates (simple or complex) and no detrimental effects on the lipid profile were shown. This study highlighted the importance of a low fat high carbohydrate diet to control obesity and its associated health problems.

Other studies are in line with the previous idea. A low fat diet with a higher carbohydrate content (of which some are sugar), in overweight subjects and with metabolic syndrome, can offer a slight loss in weight.

The large majority of epidemiological research, which has shown a positive relationship between the consumption of sugar and the prevalence of obesity, has been carried out in Europe and the United States. However, in other places it has not been possible to establish this relationship so clearly (i.e. – the



PRPPs: pyrophosphate-synthase; HPRT: Hypoxanthine-Phosphoribosyltransferase; APRT: Adenine-Phosphoribosyltransferase; XO: Xanthineoxidase; R5P: Ribose-5-phosphate; PRPP: Phosphorribosilpirofosfate; ATP:Adenosinetriphosphate; ADP:Adenosinediphosphate; AMP: Adenosinemonophosphate; GMP: Guanosine monophosphate; IMP: Inosine monophosphate.

Fig. 1. —Synthesis and degradation of purine nucleotides. Fructose is phosphorylated to fructose-1 phosphate in the liver with the contest of ATP. The consumption of AMP that can enter into the degradation path of the purine nucleotides.This degradation path culminates in the synthesis of uric acid. In the presence of oxygen (O_2) the AMPis phosphorylated into ATP. In hypoxia situations the majority of the AMP enters into the degenerative path of the purine nucleotides.

Table II

Characteristics of three published studies[13-15] regarding the relationship between the consumption of sugary drinks and obesity in different sections of the population. The first study shows a significant interaction between an important factor of our diet (sugary drinks) and the genetic predisposition towards obesity. In the following two studies, carried out on different age groups of the population, evidence was shown that the reduction of sugary drinks and diet education favoured the loss of weight

Study	*Population objective*	*Design*	*Results*
QJ et al. *N Engl J Med* 2012; 367: 1387-96	Adults (≥ 18 yrs) Interaction of sugary drinks with binomial genetic obesity	Cohort Prospective	Genetic-obesity relation modified due to consumption of sugary drinks
Janne C et al. *N Engl J Med* 2012; 367: 1397-406	from 4 to 11 years Replacement masked as sugar and weight gain	Cohort Prospective Double blind	Replacement of SD or non sugar reduces weight gain
Ebbeling et al. *N Engl J Med* 2012; 367: 1407-16	From 14 to 16 years Lifestyle-obesity relationship	Cohort Prospective	Lifestyle intervention reduction of body weight

SD: Sugary drinks.
All results shown were statistically significant.

Australian paradox)[14]. In Australia tendencies towards obesity and the consumption of sugar in the last 30 years have been put together and contrasts with what has been observed in the United Kingdom and the United States. The results confirm that in a set period, in Australia a substantial drop in the intake of sugars occurred, and during this same period obesity experimented a significant increase. In other words, the efforts made to reduce the consumption of sugar can reduce its consumption but cannot control the incidence of obesity.

Alternatively, the OMS report regarding Diet, Food and the Prevention of Chronic Diseases presented in 2003, does not show scientific evidence correlating the consumption of sugar with obesity. The same conclusion was reached by the *Institute of Medicine* in 2002, a conference of experts from the FAO and WHO in 1998, and a conference which took place in the EU in 2001. More recently, the European Food Safety Authority (EFSA) gave its opinion regarding the recommended daily carbohydrate quantities and highlighted that it was not possible to determine a top limit in the intake of sugar as there was not enough data to determine such a limit.

Threats

If excessive sugar consumption (above the recommended limits) poses a real damaging effect on health in such as it can be associated with an increase in the risk of developing obesity and suffering some form of cardiovascular disease, then why when after the consumption of similar levels of sugar some people gain weight and others not? The genetic predisposition, the different food patterns associated with the excessive consumption of sugar or the level of physical activity could explain this variability.

The genetic factors make a determining contribution to the risk of being obese. This influence oscillates between 40% and 70%[15]. Up to 32 loci have been identified as being heavily associated with the body mass index (BMI) in adults[8]. The evidence that these loci can contribute / determine the BMI in infancy and adolescence is always increasing. Even some loci could be affected by weight change during the lifespan. That is to say that the BMI of an adolescent tends to be similar in adulthood; obese and overweight adolescents are likely to be so too in adulthood. Not only that, studies also exist which show that certain genotypes can explain part of the variability which can be observed in the BMI and in the percentage or distribution of body fat. The understanding of the different mechanisms that determine the increase of weight during infancy and adolescence until reaching adulthood is important, from a clinical and preventative perspective. This knowledge could offer very useful information in relation to the possible extenuating effects (such as physical activity or personalised diets), which can have the capacity to modify the genetic protagonist.

Alternatively, the excess of fat is one of the main factors in the risk of developing resistance to insulin and obesity. Fats are not as abundant in nature as carbohydrates but, do in fact produce more than double the amount of energy. Furthermore, they are easy to store as an energy reserve for times of scarcity of carbohydrates. Despite their consumption having dropped in developed countries[9], the main surveys in Spanish cities, and of almost all Western countries, highlight still, the excessive intake of fat in the general population of adults and children (above 40% in both), far from the established recommendations. This then makes us question the relationship between the excessive consumption of fat, still present in our population and obesity.

Another factor which can be a threat for the general claim (sugar-cardiovascular disease) is the changes in the intestinal flora. It has been claimed that substantial variations in the microbial intestinal community could constitute an environmental cause for being overweight and obesity. These changes can also happen as a cause of obesity, and in particular an unbalanced diet, which often is accompanied by excess weight. In animal experiments a high fat diet can induce changes in the intestinal flora, independently from the coexistence of obesity. In humans, obesity has been associated to a reduced diversity and change in the intestinal flora, but the differences observed are not homogenous between the different studies.

One very relevant factor that could question the sugar-cardiovascular disease relationship is a sedentary lifestyle. There are indicators which show clearly that our society is getting ever more sedentary. One of the most relevant indicators is the number of hours that we watch television, as is the number of television viewers. Another indicator that is growing quickly is the growing use of the Internet and "screens" in general. The majority of these indirect indicators of a sedentary lifestyle, and, of their growing tendency, reinforce the importance of a reduction of energy expenditure as a pathogenic element over which obesity is dependent.

Therefore, there are still a lot of uncertainties to determine which factor is the most influential for excess weight; elements other than sugar that contribute to obesity exist without doubt.

Opportunities

If the increase of sugar consumption above the recommended quantities is associated with an increase in the factors of vascular risk and of cardiovascular disease, then health professionals have at their disposal a great opportunity to change this occurrence. To overcome this problem effectively we should consider that

Fig. 2.—A cartoon by Summers which reflects how in the personalised services sector (i.e. – medical consultations) the level of satisfaction is in relation to the time spent listening, understanding and formulating recommendations.

any food, consumed to excess, could carry nutritional imbalances as well as impacting negatively on the state of health for which it is never advisable. We should know the current recommendations regarding the consumption of different groups of foods in the context of a balanced and healthy diet, in order to avoid possible changes which can lead to potential negative effects on your health.

Which external circumstances can reduce the excessive consumption of sugar in our society? Fundamentally, the empathy and education of dietary habits.

In the personalised services sector (i.e. - medical consultations) the level of satisfaction is in relation to time spent listening, understanding and formulating recommendations. This has been shown in multiple ways (Fig. 2).

At a family level, it is necessary to instill the basis of a balanced diet, promoting healthy eating, limiting non desirable or unhealthy ones (excessive consumption of sugar, fats, protein, pre-cooked foods, etc.) and promoting regular physical exercise.

At school, a fundamental objective is to instill dietary and lifestyle habits.

Until now, the campaigns that have taken place in the health education arena have been of an isolated Nature, with modest results. One of the possible reasons that can justify this failure is that the determining principles for which the population changes its

Fig. 3.—Sweets and dried fruits stand in a shopping centre. In the foreground one can see play trucks (white arrows) that contain these products (the trucks are used as packaging) Buying and consuming sweets is pleasant because it brings pleasure at any time of the day (i.e. an ice-cream, a summer product, now can be consumed all year round).

dietry habits and increases activity are not educational but environmental (Fig. 3). In other words there is a socio-economic and cultural background, which determine the different types of impact of the preventative campaigns. Publicity campaigns for sugary drinks and foods with a high sugar content, the presence of vending machines with high energy products in schools and colleges, the lack of areas to practice physical exercise in cities, or the ever rising price of fruit and vegetables are some of the limiting factors.

Recommendations

The key question is determining the proportion of sugar to be taken daily within the framework of a healthy and balanced diet.

With this objective in mind, the American Heart Association (AHA) recommends the reduction of energy intake from added sugars to 100-150 kcal/day, which expressed in grams of sugar daily is 25-37.5 (no more than six teaspoons per day)

In the same country, the Institute of Medicine recommends that up to a total of 25% of total consumed calories can come from sugar.

In any case there is large variety of substances such as sweeteners either high calorie or zero calorie, that in the context of a healthy lifestyle can be chosen by consumers in function of their state of health and personal preferences.

Conclusions

Even though the intake of sugar has dropped in recent years, in our country and in the majority of developed countries, in the context of nutrition aimed at,

above all, the lowering of fat and salt intake, in order to reduce the incidence of cardiovascular diseases, the possible excessive consumption of sugar has been related to the consumption of sugary drinks, which have a clear population based target, above all in the United States: children and adolescents (Fig. 3).

A clear drop in physical exercise accompanies the current obesity epidemic, with stress as pivotal pathogenic elements and a less balanced diet.

Even with all this we cannot "criminalise" sugar as it offers so many other benefits. Even though more studies are needed, there exists a sufficient basis to design strategies for public health with a view to reducing the excessive consumption of sugary drinks, as part of a healthy lifestyle. Maybe paying attention to other important aspects of our habits (playing sport, avoiding excessive animal fats, not ingesting toxins etc.) we can contribute in reducing the incidence of vascular and cardiovascular disease risk factors, and, without fear, look for the "right sugar to sweeten our lives".

References

1. www.historiacocina.com/es/historia-del-azucar. (Consultado en 30 de Octubre de 2012).
2. Thornley S, Tayler R, Sikaris K. Sugar restriction: the evidence for a drug-free intervention to reduce cardiovascular disease risk. *Intern Med J* 2012; 42 (Suppl. 5): 46-58.
3. Castell MV , Martínez MÁ, Sanz J , García Puig J. Prevalencia, conocimiento y control de la hipertensión arterial en la población española. El estudio MADRIC. *Med Clin* 2010; 135: 671-2.
4. Rosado Martín J, Martínez López MªA, Mantilla Morato T, Dujovne Kohan I, Palau Cuevas FJ, Torres Jiménez R, García Puig J, en representación del grupo MAPA-Madrid. Prevalencia de diabetes en una población adulta de Madrid (España). *Gaceta Sanit* 2011; 26: 243-50.
5. Gabriel R, Alonso M, Segura A, Tormo MJ, Artiago LM, Banegas JR et al. Prevalencia, distribución y variabilidad geográfica de los principales factores de riesgo cardiovascular en España. Análisis agrupado de datos individuales de estudios epidemiológicos poblacionales: estudio ERICE. *Rev Esp Cardiol* 2008; 61: 1030-40.
6. Soriguer F, Goday A, Bosch-Comsas A, Bordiú E, Calle Pascual A, Carmena R et al. Prevalence of diabetes mellitus and impaired glucose regulation in Spain: the Di@bet.es study. *Diabeteología* 2012; 55: 88-93.
7. Torres Jiménez R, García Puig J. Disfunción endotelial e hiperuricemia: papel de la enzima Xantina oxidasa. *Rev Clin Esp* 2002; 202: 549-51.
8. Qibin Q, Audrey Y, Kang J, Jense MK, Curhan GC and Pasquale LR. Sugar-sweetened beverages and genetic risk of obesity. *N Engl J Med* 2012; 367: 1387-96.
9. Ruyter J, Olthof MR, Seidell JC and Katan MB. A trial of sugar-free or sugar-sweetened beverages and body weight in children. *N Engl J Med* 2012; 367: 1397-406.
10. beling CB, Feldman H and Chomitz VR. A Randomized trial of sugar-sweetened beverages and adolescent body weight. *N Engl J Med* 2012; 367: 1407-16.
11. Grundt JH, Nakling J, Eide GE, Markestad T. Possible relation between maternal consumption of added sugar and sugar-sweetened beverages and birth weight — time trends in a population. *BMC Public Health* 2012; 12: 901.
12. Fortuna JL. The obesity epidemic and food addiction: clinical similarities to drug dependence. *J Psychoactive Drugs* 2012; 44: 56-63.
13. Saris WH, Astrup A, Prentice AM, Zunft HJ, Formiguera X, Verboeket-van de Venne WPet al. Randomized controlled trial of changes in dietary carbohydrate/fat ratio and simple vs. complex carbohydrates on body weight and blood lipids: the CARMEN study. The Carbohydrate Ratio Management in European National diets. *J Obes Relat Metab Disord* 2000; 24: 1310-8.
14. Barclay AW, Brand-Miller J. The Australian paradox: a substantial decline in sugars intake over the same timeframe that overweight and obesity have increased. *Nutrients* 2011; 3: 491-504.
15. Bell CG, Walley AJ, Froguel P. The genetics of human obesity. *Nature Reviews Genetics* 2005; 6: 221-34.