



## **Implication of Sugar Intake in Haemorrhoid and Menstruation**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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### **ABSTRACT**

This review discusses the implication of sugar intake in haemorrhoid and menstruation. Haemorrhoid is the clustering of veins in the rectum leading to swollen anus. This occurs due to pressure exerted on the rectum. When these veins swell, they expand outward into the membranes around the rectal and anal tissue. Most people believed that sugar is the onset of haemorrhoid. Haemorrhoid occurs as a result of pressure exerted on the rectum leading to the swelling of the veins in the rectum. Since sugar does not exert pressure on the rectum, it doesn't cause haemorrhoid but can aggravate it and increase the grade. To reduce or avoid haemorrhoid, it is advisable to visit the toilet and excrete as soon as one is pressed. The rectum should not be allowed to be filled for a long time. Menstruation is the regular monthly discharge of blood and mucosal tissue from the inner lining of the uterus through the vagina. This stops after menopause, which usually occurs between 45 and 55 years of age. It also stops during pregnancy and typically do not resume during the initial months of breastfeeding. There is a general believe that sugar

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intake increases menstrual flow but this review shows otherwise. High intake of sugar has not been implicated in increasing menstrual flow but cause increased severe menstrual cramps by increasing the production of prostaglandins. Prostaglandins act by contracting the uterine walls and constricting the blood vessels of the uterus which results in pain during menstruation.

*Keywords: Sugar; haemorrhoid; menstruation; prostaglandins.*

## 1. INTRODUCTION

Sugar is the generic name for sweet-tasting, soluble carbohydrates, many of which are used in food [1]. The various types of sugar are derived from different sources. Simple sugars are called monosaccharides and include glucose (also known as dextrose), fructose and galactose. Table sugar or granulated sugar refers to sucrose, a disaccharide of glucose and fructose. Other disaccharides include maltose (from malted grain) and lactose (from milk). Longer chains of sugars are called oligosaccharides or polysaccharides. Excessive consumption of sugar has been implicated in the onset of obesity, diabetes, cardiovascular disease, dementia, and tooth decay [2].

Scientifically, sugar loosely refers to a number of carbohydrates, such as monosaccharides, disaccharides or oligosaccharides. The names of typical sugars end with -ose, as in glucose and fructose. The acyclic mono- and disaccharides contain either aldehyde groups or ketone groups. These carbon-oxygen double bonds (C=O) are the reactive centres. All saccharides with more than one ring in their structure result from two or more monosaccharides joined by glycosidic bonds with the resultant loss of a molecule of water [3]. Monosaccharides in a closed-chain form can form glycosidic bonds with other monosaccharides, creating disaccharides (such as sucrose) and polysaccharides (such as starch). Enzymes must hydrolyse or otherwise break these glycosidic bonds before such compounds become metabolized [4]. In these closed-chain forms, the aldehyde or ketone group remains non-free, so many of the reactions typical of these groups cannot occur. Glucose in solution exists mostly in the ring form at equilibrium. Because sugars burn easily when exposed to flame, the handling of sugars risks dust explosion. The risk of explosion is higher when the sugar has been milled to superfine texture, such as for use in chewing gum [5]. The 2008 Georgia sugar refinery explosion, which killed 14 people and injured 40, and destroyed most of the refinery, was caused by the ignition of sugar dust. In its culinary use, exposing sugar

to heat causes caramelization. As the process occurs, volatile chemicals such as diacetyl are released, producing the characteristic caramel flavour [2].

Various biochemical processes responsible for the metabolic formation, breakdown and inter-conversion of carbohydrates in living organisms. Carbohydrates are central to many essential metabolic pathways [6]. Plants synthesize carbohydrates from carbon dioxide and water through photosynthesis, allowing them to store energy absorbed from sunlight internally [3]. When animals and fungi consume plants, they use cellular respiration to break down these stored carbohydrates to make energy available to cells. Both animals and plants temporarily store the released energy in the form of high energy molecules, such as ATP, for use in various cellular processes [3].

Although humans consume a variety of carbohydrates, digestion breaks down complex carbohydrates into a few simple monomers (monosaccharides) for metabolism [7]. Glucose constitutes about 80% of the products, and is the primary structure that is distributed to cells in the tissues, where it is broken down or stored as glycogen [7]. In aerobic respiration, the main form of cellular respiration used by humans, glucose and oxygen are metabolized to release energy with carbon dioxide and water as by-products [3]. Most of the fructose and galactose travel to the liver, where they can be converted to glucose [7].

Glucoregulation is the maintenance of steady levels of glucose in the body. Hormones released from the pancreas regulate the overall metabolism of glucose. Insulin and glucagon are the primary hormones involved in maintaining a steady level of glucose in the blood, and the release of each is controlled by the amount of nutrients currently available. The amount of insulin released in the blood and sensitivity of the cells to the insulin both determine the amount of glucose that cells break down [7]. Increased level of glucagon activates the enzymes that catalyse glycogenolysis, and inhibits the enzymes that

catalyze glycogenesis [8]. Conversely, glycogenesis is enhanced and glycogenolysis inhibited when there are high levels of insulin in the blood [8].

The level of circulatory glucose (known informally as "blood sugar") is the most important factor determining the amount of glucagon or insulin produced. The release of glucagon is precipitated by low levels of blood glucose, whereas high levels of blood glucose stimulates cells to produce insulin. Because the level of circulatory glucose is largely determined by the intake of dietary carbohydrates, diet controls major aspects of metabolism via insulin [4].

A technical report by the world health organization (WHO) provided evidence that high intake of sugary drinks (including fruit juice) increased the risk of obesity by adding to overall energy intake. The "empty calories" argument states that a diet high in added sugar will reduce consumption of foods that contain essential nutrients. By itself, sugar is not a factor causing obesity and metabolic syndrome, but rather when over consumed is a component of unhealthy dietary behaviour. Meta-analyses showed that excessive consumption of sugar-sweetened beverages increased the risk of developing type II diabetes and metabolic syndrome including weight gain and obesity in adults and children [6].

Some studies report evidence of causality between high consumption of refined sugar and hyperactivity. One review of low-quality studies of children consuming high amounts of energy drinks showed association with higher rates of unhealthy behaviours, including smoking, alcohol abuse, and insomnia. The WHO report stated that "Sugars are undoubtedly the most important dietary factor in the development of dental caries". Claims have been made of a sugar–Alzheimer's disease connection, but there is inconclusive evidence that cognitive decline is related to dietary fructose or overall energy intake [9].

## 2. HAEMORRHOID

Haemorrhoids, also called piles which are vascular structures in the anal canal. Haemorrhoids happen when clusters of veins in the rectum or anus get swollen (or dilated) due to pressure exerted on the rectum. When these veins swell, they begin to expand outward into the membranes around the rectal and anal tissue. This can become uncomfortable or

painful. Haemorrhoids are not always visible, but when they expand, they can look like red or discoloured bumps or lumps [10].

### 2.1 Types of Haemorrhoid

There are four (4) types of haemorrhoids and they include [11].

### 2.2 Internal Haemorrhoids

Internal haemorrhoids are found in the rectum. They can't always be seen because they're too deep in the anus to be visible .Internal haemorrhoids aren't normally serious and tend to go away on their own. Sometimes internal haemorrhoids can swell and stick out of the anus. There aren't any nerves that detect pain in the rectum, but they can cause symptoms if they grow larger, including [12]:

- Pain or discomfort.
- Itching.
- Burning.
- Noticeable lumps or swelling near the anus.

Faeces traveling through the rectum can also irritate an internal haemorrhoid. This can cause bleeding that might be noticeable on toilet tissue [12].

### 2.3 External Haemorrhoids

External haemorrhoids occur on the anus, directly on the surface of where the bowel movements come out. They're not always visible, but are sometimes seen as lumps on the anal surface. External haemorrhoids aren't usually a serious medical issue [11]. The symptoms of external haemorrhoids are essentially the same as those of internal ones. But since they're located on the outside of the rectal area, there might be more pain or discomfort when sitting down, doing physical activities, or having a bowel movement. They're also easier to see when they swell, and the bluish colour of the dilated veins is visible beneath the anal skin surface [12].

### 2.4 Prolapsed Haemorrhoids

A prolapsed haemorrhoid occurs when internal haemorrhoids swell and stick out of the anus. Grades are assigned to a prolapsed haemorrhoid based on how far it sticks out [11,12]:

- **Grade one:** Not prolapsed at all.
- **Grade two:** Prolapsed, but will retract by themselves. These may only prolapse when there is pressure on the anal or rectal area, such as by straining when having a bowel movement, and then return to their normal position afterward.
- **Grade three:** Prolapsed, and it can be pushed back in. These may need to be treated so that they don't become too painful or infected.
- **Grade four:** Prolapsed, and it can't be pushed back in without a lot of pain. These will usually need to be treated to prevent pain, discomfort, or further complications.

Prolapsed haemorrhoids look like swollen red lumps or bumps outside the anus. Prolapsed haemorrhoids may have no other symptoms than the protrusion but they may cause pain, discomfort, itchiness, or burning [11].

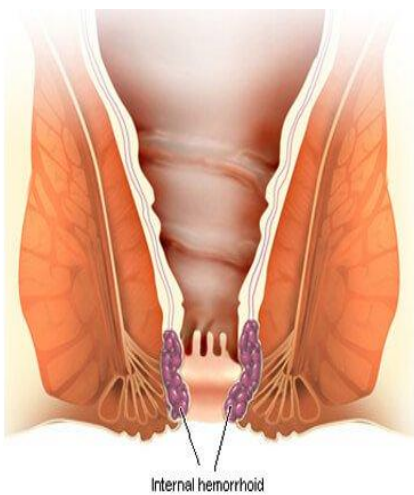


Fig. 1. Structure of Internal Haemorrhoid [11]

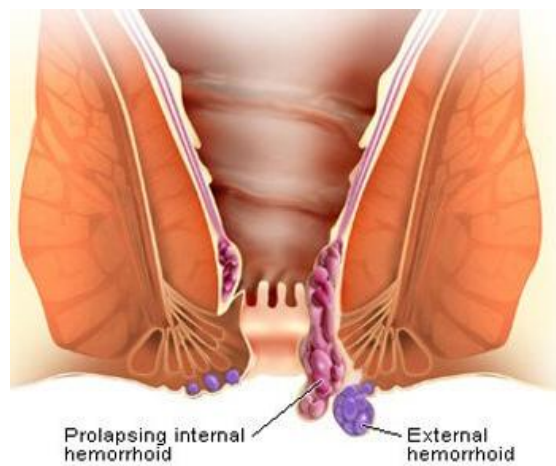


Fig. 2. Structure of External Haemorrhoid [11]

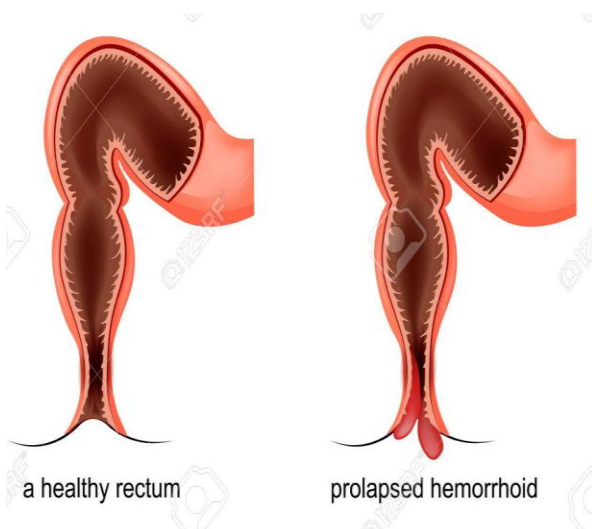


Fig. 3. Structure of Prolapsed Haemorrhoid [11]



Fig. 4. Structure of Thrombosed Haemorrhoid [11]

## 2.5 Thrombosed Haemorrhoids

A thrombosed haemorrhoid contains a blood clot (thrombosis) within the haemorrhoid tissue. They may appear as lumps or swelling around the anus [11]. Thrombosed haemorrhoids are essentially a complication of a haemorrhoid, in which a blood clot forms. Blood clots can happen in both internal and external haemorrhoids and the symptoms may include [12]:

- Intense pain and itchiness
- swelling and redness
- bluish colour around area of haemorrhoid

## 2.6 Causes of Haemorrhoid

The veins around the anus tend to stretch under pressure and may bulge or swell. Swollen veins (haemorrhoids) can develop from increased pressure in the lower rectum due to [13]:

- Straining during bowel movements
- Sitting for long periods of time on the toilet
- Chronic diarrhoea or constipation
- Obesity
- Pregnancy
- Anal intercourse
- Low fibre diet
- Pelvic floor dysfunction
- Squatting while defecating
- Genetics
- Absence of valves within the haemorrhoidal veins
- Lack of exercise
- Aging because the tissues that support the veins in the rectum and anus can weaken and stretch.
- Irregular bowel habits

## 2.7 Signs and Symptoms of Haemorrhoids

Seeing blood in the toilet bowl after a bowel movement is no doubt alarming, but it's one of the main symptoms of haemorrhoids. Other symptoms include [13]:

- Painless bleeding during bowel movements.
- There might be itching or irritation on the anal region.
- Pain or discomfort swelling around the anus.

- A lump near the anus, which may be sensitive or painful.
- Bright red blood on toilet paper or in stool after a bowel movement.

## 2.8 Pathophysiology of Haemorrhoid

Haemorrhoid cushions are a part of normal human anatomy and become a pathological disease only when they experience abnormal changes. There are three main cushions present in the normal anal canal [14]. These are located classically at left lateral, right anterior, and right posterior positions. They are composed of neither arteries nor veins, but blood vessels called sinusoids, connective tissue, and smooth muscle [15]. Sinusoids do not have muscle tissue in their walls, as veins do. This set of blood vessels is known as the haemorrhoidal plexus [15].

Haemorrhoid cushions are important for continence. They contribute to 15–20% of anal closure pressure at rest and protect the internal and external anal sphincter muscles during the passage of stool. When a person bears down, the intra-abdominal pressure grows, and haemorrhoid cushions increase in size, helping maintain anal closure. Haemorrhoid symptoms are believed to result when these vascular structures slide downwards or when venous pressure is excessively increased [16]. Increased internal and external anal sphincter pressure may also be involved in haemorrhoid symptoms. Two types of haemorrhoids occur: internals from the superior haemorrhoidal plexus and externals from the inferior haemorrhoidal plexus the dentate line divides the two regions.

## 2.9 Prevention of Haemorrhoid

Prevention of haemorrhoid includes [17]:

- **Eat high-fibre foods:** Eat more fruits, vegetables and whole grains. Doing so softens the stool and increases its bulk, which will help avoid the straining that can cause haemorrhoids. Add fibre to diet slowly to avoid problems with gas.
- **Drink plenty of fluids:** Drink six to eight glasses of water and other liquids (not alcohol) each day to help keep stools soft.
- **Don't strain:** Straining and holding breath when trying to pass a stool creates greater pressure in the veins in the lower rectum.

- **Go as soon as you feel the urge:** Passing of bowel movement should not be delayed so that the stool does not become dry and get harder to pass out.
- **Exercise:** Stay active to help prevent constipation and to reduce pressure on veins, which can occur with long periods of standing or sitting. Exercise can also help to lose excess weight that may be contributing to haemorrhoids.
- **Avoid long periods of sitting:** Sitting too long, particularly on the toilet, can increase the pressure on the veins in the anus.

### 3. MENSTRUATION

Menstruation is the regular monthly discharge of blood and mucosal tissue (known as menses) from the inner lining of the uterus through the vagina [18]. Menstruation stops occurring after menopause, which usually occurs between 45 and 55 years of age [19]. Periods also stop during pregnancy and typically do not resume during the initial months of breastfeeding. Menstruation involves highly complex hormonal interactions. The key hormones involved in menstruation are oestrogen and progesterone (produced by the ovaries) and luteinising hormone and follicle stimulating produced by the pituitary gland, under the influence of hormones secreted by the hypothalamus [20]. The interactions between these organs are

referred to as the hypothalamic-pituitary ovarian axis (HPO axis).

### 3.1 Menstrual Cycle

The menstrual cycle is the regular natural change that occurs in the female reproductive system (specifically the uterus and ovaries) that makes pregnancy possible [21,22]. The cycle is required for the production of oocytes, and for the preparation of the uterus for pregnancy [23]. The menstrual cycle occurs due to the rise and fall of hormones, this cycle results in the thickening of the lining of the uterus, and the growth of an egg, (which is required for pregnancy). The egg is released from an ovary around day fourteen in the cycle; the thickened lining of the uterus provides nutrients to an embryo after implantation, if pregnancy does not occur, the lining is released in what is known as menstruation [24]. During the remainder of the menstrual cycle the uterine lining regrows. It does so in preparation for pregnancy, which occurs if the egg (oocyte) a woman releases about half way through her menstrual cycle is fertilised. When fertilisation occurs, the lining stays in place to nourish the fertilised egg. When fertilisation does not occur the menstrual cycle continues and the uterine lining is shed marking the start of the woman's next menstrual period. The menstrual cycle is governed by hormonal changes. These changes can be altered by using hormonal birth control to prevent pregnancy [20].

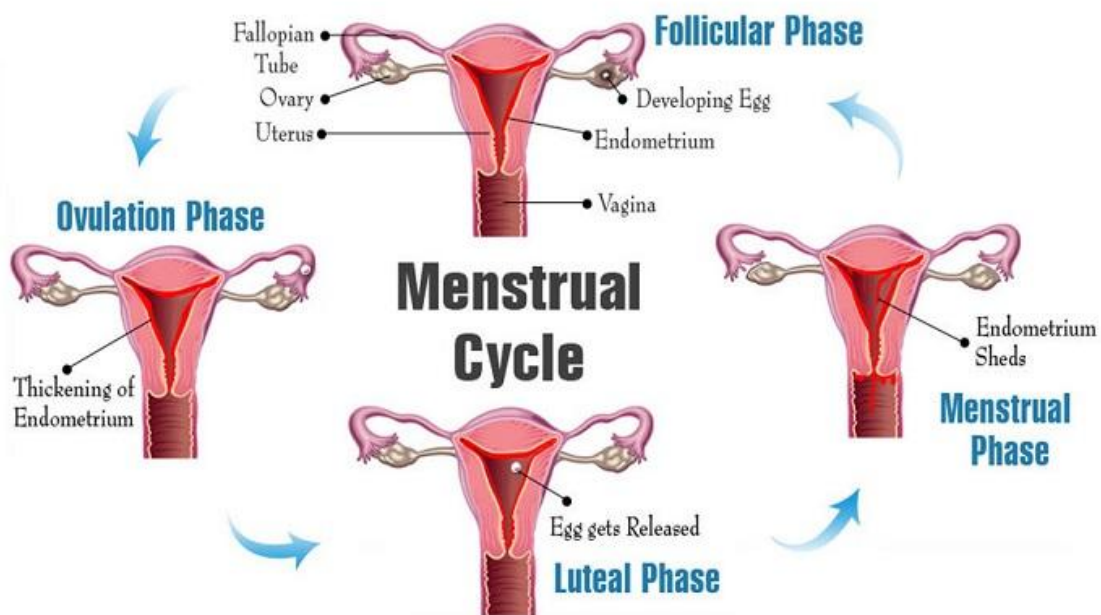


Fig. 5. Menstrual Cycle [25]

In most women, various physical changes are brought about by fluctuations in hormone levels during the menstrual cycle. This includes muscle contractions of the uterus (menstrual cramping) that can precede or accompany menstruation. Some may notice water retention, changes in sex drive, fatigue, breast tenderness, or nausea [26]. Breast swelling and discomfort may be caused by water retention during menstruation [27]. Usually, such sensations are mild, and some females notice very few physical changes associated with menstruation. A healthy diet, reduced consumption of salt, caffeine and alcohol, and regular exercise may be effective for women in controlling some symptoms. Severe symptoms that disrupt daily activities and functioning may be diagnosed as premenstrual dysphoric disorder [20,28].

Many women experience painful cramps, also known as dysmenorrhea, during menstruation. Pain results from ischemia and muscle contractions. Spiral arteries in the secretory endometrium constrict, resulting in ischemia to the secretory endometrium. This allows the uterine lining to slough off. The myometrium contracts spasmodically in order to push the menstrual fluid through the cervix and out of the vagina. The contractions are mediated by a release of prostaglandins [22].

#### **4. IMPLICATION OF SUGAR INTAKE IN HAEMORRHOID AND MENSTRUATION**

##### **4.1 Implication of Sugar Intake in Haemorrhoid**

Haemorrhoid occurs when pressure is exerted on the rectum leading to the swelling of the rectal veins. Several things can exert pressure on the rectum but high intake of sugar is not one of those factors that exert pressure on the rectum. Since high intake of sugar doesn't exert pressure on the rectum then sugar doesn't cause haemorrhoid. But it has been found out that haemorrhoid can be implicated by sugar because it aggravates the pain caused by haemorrhoid and makes haemorrhoid last longer than it should last [29,30].

As haemorrhoid increase in grades, the harder it is to be cured; hence, sugar increases the grade of haemorrhoid. Although it hasn't been found out how sugar increases the grade of haemorrhoid but it is a factor that aggravates haemorrhoid. Normally haemorrhoid can exist in

four forms; internal, external, prolapsed and thromboses. The less severe form of haemorrhoid is the internal haemorrhoid in which the swelling of the veins is not visible it occurs in the rectum [31]. High intake of sugar can increase the severity of internal haemorrhoid making it more painful and difficult to cure. Internal haemorrhoid is in grades, the effect of high intake of sugar on internal haemorrhoid is increasing the grades at which the haemorrhoid existed thereby occurring with more pain and difficulty to cure. The main thing sugar does to haemorrhoid is to increase and aggravate the grade of haemorrhoid and makes it worse thereby causing great pain [30].

##### **4.2 Implication of Sugar Intake in Menstruation**

During menstruation, high intake of sugar leads to severe menstrual cramps. The severe cramps is as a result of high production of prostaglandins because of high intake of sugar. High intake of sugar leads to increased production of prostaglandins and prostaglandins cause inflammation and pain aside from the good functions of prostaglandins [32]. These prostaglandins cause menstrual cramps by contracting the walls of the uterus. It has been reported that D-glucose and medically inert osmotic compounds increase the prostanoil production in human mesothelial cells [33].

A high concentration of glucose significantly increases the level of thymidine incorporation, the level of 5-bromo-2-deoxyuridine incorporation and the number of cells. Moreover, high glucose increases the intracellular reactive oxygen species, phosphorylation of the cytosolic phospholipase A<sub>2</sub> and the release of arachidonic acid. In addition, high glucose also increases the level of cyclooxygenase-2 (COX-2) protein expression which stimulates the synthesis of prostaglandins [34]. Subsequently, high glucose induced prostaglandins stimulated Peroxisome proliferator-activated receptors (PPAR) expression directly or through Akt phosphorylation indirectly through the E type prostaglandins receptor. The COX 1 and 2 expression is examined as a function of the time to determine whether high glucose can induce the expression of COX 1 and 2 proteins [35]. It was concluded that high glucose levels increased the level of COX 2 expression in a time dependent manner but had no effect on COX 1. Prostaglandins are synthesized from lipids eicosanoids [36].

## 5. CONCLUSION

Haemorrhoid is the clustering of veins in the rectum leading to swollen anus. This occurs due to pressure exerted on the rectum. When these veins swell, they expand outward into the membranes around the rectal and anal tissue. Most people believed that sugar is the onset of haemorrhoid. Haemorrhoid occurs as a result of pressure exerted on the rectum leading to the swelling of the veins in the rectum. Since sugar does not exert pressure on the rectum, it doesn't cause haemorrhoid but can aggravate it and increase the grade. To reduce or avoid haemorrhoid, it is advisable to visit the toilet and excrete as soon as one is pressed. The rectum should not be allowed to be filled for a long time. Menstruation is the regular monthly discharge of blood and mucosal tissue from the inner lining of the uterus through the vagina. This stops after menopause, which usually occurs between 45 and 55 years of age. It also stops during pregnancy and typically do not resume during the initial months of breastfeeding. There is a general believe that sugar intake increases menstrual flow but this review shows otherwise. High intake of sugar has not been implicated in increasing menstrual flow but cause increased severe menstrual cramps by increasing the production of prostaglandins. Prostaglandins act by contracting the uterine walls and constricting the blood vessels of the uterus which results in pain during menstruation.

## CONSENT AND ETHICAL APPROVAL

As per university standard guideline participant consent and ethical approval has been collected and preserved by the authors.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

- Claire BH, Kretchmer N. Sugars and Sweeteners. *CRC Press, Inc.* 1991;22: 9–10.
- Edwards WP. *The Science of Sugar Confectionery.* Royal Society of Chemistry. 2015;18.
- Nelson DL. *Lehninger principles of biochemistry.* New York. W.H. Freeman and Company. 2013;20:224-229.
- Brockman RP. Roles of glucagon and insulin in the regulation of metabolism in ruminant, a review. *The Canadian Veterinary Journal.* 1978;19(3):55–62.
- Buss D, Robertson J. *Manual of Nutrition;* Ministry of Agriculture, Fisheries and Food. London. Her Majesty's Stationery Office. 1976;42:5–9.
- Maughan R. *Carbohydrate metabolism.* Surgery (Oxford). 2009;27(1):6-10.
- Hall JE. *Guyton and Hall Textbook of Medical Physiology E-Book (13 ed.).* Elsevier Health Sciences. 2015;22:388-394.
- Ahern K, Rajagopal I, Tan T. *Biochemistry free for all.* Oregon State University. 2017; 41:9-12.
- Chen H. *Illustrative Handbook of General Surgery.* Berlin. Springer. 2010;31:217.
- Agte V, Joshi S. Digestibility of dietary fibre components in vegetarian men. *Plant Foods for Human Nutrition (Dordrecht, Netherlands).* 1995;48(1):39–44.
- Abramowitz L, Batallan A. Epidemiology of anal lesions (fissure and thrombosed external hemorrhoid) during pregnancy and postpartum. *Gynecol Obstet Fertil.* 2003;31 (6):546–549.
- Abramowitz L, Benifla JL, Daraï E, Mignon M, Sobhani I, Vuagnat A. Anal fissure and thrombosed external hemorrhoids before and after delivery. *Dis Colon Rectum.* 2002;45(5):650–655.
- Horton D, Pigman W. *Pigman and Horton,* ed. *The Carbohydrates: Chemistry and Biochemistry (2<sup>nd</sup> ed.).* San Diego. Academic Press. 1972;1:1–67.
- Lorenzo RS. "Hemorrhoids: diagnosis and current management". *Am Surg.* 2009;75 (8):635–642.
- Beck DE. *The ASCRS textbook of colon and rectal surgery (2<sup>nd</sup> ed.).* New York. Springer. 2011;15:175.
- Davies RJ. "Haemorrhoids". *Clinical evidence.* 2006;23(15):711–724.
- Gitzelmann R, Hansen RG. *Physiological Effects of Food Carbohydrates.* American Chemical Society (ACS) Symposium Series. 1975;15:100–122.
- Goldenring JM. "All About Menstruation". *WebMD.* 2007;26:435–438.
- Malhotra C, Saha R, Sharma P, Taneja DK. "Problems related to menstruation amongst adolescent girls". *Indian J Pediatr.* 2008;75(2):125–129.
- Czyzyk A, Katulski K, Maciejewska J, Meczekalski B, Podfigurna S. "Functional



- hypothalamic amenorrhea and its influence on women's health". *Journal of Endocrinological Investigation*. 2014;37(11):1049–1056.
21. Silverthorn DU. *Human Physiology. An Integrated Approach* (6<sup>th</sup> ed.). Glenview, IL: Pearson Education. 2013;44:850–890.
  22. Sherwood L. *Human Physiology: From Cells to Systems* (8<sup>th</sup> ed.) Belmont, California. Cengage. 2013;32:735–794.
  23. Ecochard R, Gougeon A. Side of ovulation and cycle characteristics in normally fertile women. *Human Reproduction*. 2000;15(4):752–755.
  24. Karapanou O, Papadimitriou A. "Determinants of menarche". *Reproductive Biology and Endocrinology*. 2010;8:115.
  25. Gray HD. "The Ovum". *Anatomy of the human body*. 2000;41:345–350.
  26. Kaidar PO, Person B, Wexner SD. "Hemorrhoidal disease. A comprehensive review" (PDF). *Journal of the American College of Surgeons*. 2007;204(1):102–117.
  27. Mishra G, Jones M, Ju H. "The prevalence and risk factors of dysmenorrhea". *Epidemiologic Reviews*. 2014;36(1):104–113.
  28. Catt KJ, Feng H, Gustofson RL, Hu L, Krsmanovic LZ, Leung PK, Mores N. "Converse regulatory functions of estrogen receptor-alpha and -beta subtypes expressed in hypothalamic gonadotropin-releasing hormone neurons". *Mol. Endocrinol*. 2008;22(10):2250-2255.
  29. Dugalic V, Gojnic M, Milicevic S, Papic M, Pervulov M, Vidakovic S. The significance of detailed examination of hemorrhoids during pregnancy. *Clin Exp Obstet Gynecol*. 2005;32(2):183–184.
  30. Dashty M. A quick look at biochemistry: Carbohydrate metabolism. *Clinical Biochemistry*. 2013;46(15):1339–1352.
  31. Connor P, Hadden L, Marriott BP, Olsho L. Intake of added sugars and selected nutrients in the United States, National Health and Nutrition Examination Survey. *Crit Rev Food Sci Nutr*. 2010;50(3):228–258.
  32. Miller L, Notter KM. "Menstrual reduction with extended use of combination oral contraceptive pills: Randomized controlled trial". *Obstetrics and Gynecology. LWW Journal*. 2001;98(5):771–778.
  33. Giannini AJ, Price WA. Binge eating during menstruation. *The Journal of Clinical Psychiatry*. 1983;44(11):431.
  34. Schade RR, Schubert MC, Sridhar S, Wexner SD. What every astroenterologist needs to know about common anorectal disorders. *World J Gastroenterol*. 2009;15(26):3201–3209.
  35. Weschler T. *Taking Charge of Your Fertility* (Revised ed.). New York: Harper Collins. 2002;23:359–361.
  36. Airaodion AI, Ogbuagu U, Ogbuagu EO, Oloruntoba AP, Agunbiade AP, Airaodion, EO, Mokelu IP, Ekeh SC. Mechanisms for Controlling the Synthesis of Lipids – Review. *International Journal of Research*. 2019;6(2):123-135.

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