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The effect of hot water and traditional yeast on aorta inflammation induced by refined crystallize sugar

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Allah is the safety in the mess of this life ,when you feel that all roads are closed , Allah's kindness will come to you from the impossible path.

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Dedication

Allah will open a door that you desperately thought never even had a key ,I am so thankful to the greatest Allah .

اللهم لك الحمد حتى ترضى و لك الحمد اذا رضيت و لك الحمد بعد الرضا.

Family is the shield that protect you during rough times.

To my parents AyachiTayeb ,GheriebWided thank you for helping me to shape my life with positivity and love,thank you for understanding me without speaking , thank you for your support, all the words of thanks cannot describe my feelings ,thank you for every think, without you I would never been the person I am today .

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Dear me, thank you for doing your best , don't allow anyone to trigger you , let it go walk away ,you'll be proud of yourself later

DJIHANE

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AssalaMelek.

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ListofAbbreviations

AGP Acid glucoprotein

CCL3 Chemokine ligand 3

CCR7 Chemokine receptor 7

CRP C-reactive protein

Cv Cardiovascular

DCs Dendritic cells

DP Degree of polymerization

ECs Endothelial cells

ECG Electrocardiogram

ESR Erythrocyte sedimentation rate

FC Crystallized fragment

FCɣR Crystallized factor gamma receptor

HFCS High-fructose corn syrup

HR Heart rate

HRV Heart rate variability

HsCRP Human's CRP

IBD Inflammatory bowel disease

ICAM Intercellular adhesion molecule-1

IFN ɣ Interferon gamma

IL- α Interleukin alpha

IL-1 β Interleukin 1 beta

IL-1 Interleukin1

IL-10 Interleukin 10

IL-12 Interleukin 12

IL-13 Interleukin 13

IL-17 Interleukin17

IL-2 Interleukin 2

IL-4 Interleukin 4

IL-5 Interleukin 5

IL-6 Interleukin 6

IL-8 Interleukin 8

IL-9 Interleukin 9

LDL Low-density lipoprotein

Lv Left ventricular

MI Myocardial infraction

Mcrp Monomeric C-reactive protein

MMPs Matrix metalloprotéinases

NAFLD Non-alcoholic fatty liver disease

NETs Neutrophil extracellular traps

NF-Kb Nuclear factor-kappa B

NK Natural killer cells

NO Nitric oxide

PAI-1 Plasminogen active inhibitor-1

PAMPs Pathogen-associated molecular patterns

PCH Phosphocholine

pCRP Pentameric C-reactive protein

PCT Procalcitonin

PGs Prostaglandins

PMNs Pollymorphonuclear cells

Polyols Poly oligosaccharides

PRRs Pathogen recognition receptors

ROS Reactive oxygen species

SMCs Smooth muscle cells

TANs Tumor associated neutrophils

TGF- β Transforming growth factor – beta

THP-1 Tamm-Horsfall Protein 1

TLRs Toll-like receptors

TNF-α Tumor necrosis factor-alpha

T2D Type 2 diabetes

VCAM Vascular cell adhesion molecule

VCAM-1 Vascular endothelial cell adhesion molecular-1

VEGEF Vascular endothelial growth factor

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Introduction

Introduction

Sugar in many forms and permutation is ubiquitous, naturally occurring, and required for most life forms on planet earth. Sugar is used as a preservative, a viscosity-enhancing agent, a sweetening agent, and for other reasons in foods and beverages **(White, 2018)**.

High sugar intake has long been recognized as a potential environmental risk factor for increased incidence of many non-communicable diseases, including obesity, cardiovascular disease, metabolic syndrome, and type 2 diabetes (T2D) **(Xiao et al.,2022).**

The "Western diet" is highly palatable and energy-dense, containing high levels of saturated fats and processed sugars, which promote obesity. The chronic consumption of this diet is associated with various medical conditions including cardiovascular disease, gastrointestinal and respiratory difficulties, hypertension, stroke, diabetes mellitus and many types of cancers **(Beilharz et al., 2016).**

It has been postulated that dietary sugar consumption contributes to increased inflammatory processes in humans **(Della et al., 2018).**

For instance, inflammation plays an important role in most major aortic pathologies, leading to degradation of the vessel wall and potentially vessel occlusion, aneurysm formation or dissection **(Syed et al., 2018).**

Aortic aneurysm formation includes an inflammatory mediated process but is distinct from atherosclerosis because it is characterized by media atrophy rather than intimal proliferation . Consequent thinning, weakening and stiffening of the aortic wall leaves it vulnerable to dilatation and rupture **(Syed et al.,2018).**.

Furthermore, sourdough is the oldest form of leavened bread used as early as 2000 BC by the ancient Egyptians. It may have been discovered by accident when wild yeast drifted into dough that had been left out resulting in fermentation of good microorganisms, which made bread with better flavor and texture.

The discovery was continued where sourdough was produced as a means of reducing wastage with little known (at that point of time) beneficial effects to health. With the progress and advent of science and technology in nutrition, sourdough fermentation is now know to process many desirable attributes in terms of health benefits, it has become the focus of attention and practice in modern healthy eating lifestyle when linked to the secret of good health **(Siew et al., 2021).**

On the other way, the drinking hot water had a favorable impact on intestinal movement. Consumption of hot beverages stimulates the overall physiological process faster than normal rate. Drinking hot water can lubricate in the body. It will be beneficial to patients who have arthritis. Hot water can reduce the lower esophageal sphincter resting pressure and shorten the contraction duration of the esophageal body and relieve symptoms. **(Subaraman et al., 2020).**Hot water expands your arteries and veins , allowing for better blood circulation throug hout the body . This also can regulate your blood pressure levels**(Thais,2023).**

In the present study, our objectives were to:

1-evaluate the effect of sugar, traditional yeast and hot water on the weight and diet.

2-evaluate the effect of hot water and traditional yeast on the inflammation induced by high consumptin of refined crystallize sugar by measuring the C-reactive protein.

3-evaluate the benefits of hot water at 50°C and traditional yeast on some biochemical parameteres.

4- determinate histological sections on the aorta.

Bibliographic Part

Chapter I

Sugar

I-Sugars

1-Definition of sugar

Sugar is a conventional everyday concept used mainly in relation to sucrose (table sugar), as well as other water soluble simple carbohydrates with a sweet taste **(Saitkulov et al.,2022)**.

The most common sugar is sucrose, a crystalline tabletop and industrial sweetener used in foods and beverages **(Zaitouni et al., 2018)**.

The commercial sugar is the disaccharide sucrose white sugar **(Kamal and Klein, 2011)**.

The human body, and especially the brain, needs a constant supply of glucose, which ensures the effectiveness and efficiency of its work **(Saitkulov et al., 2022)**.

The majority of the natural sugars contain 6 or 12 carbon atoms in their molecules **(Kamal and Klein, 2011)**. The term dextrose is used to refer to glucose. Extrinsic or added sugar refers to sucrose or other refined sugars in soft drinks and incorporated into food, fruit drinks, and other beverages. Intrinsic or naturally occurring sugar refers to the sugar that is an integral constituent of whole fruit, vegetable, and milk products **(Howard and Wylie-Rosett, 2002)**.

Many food which contain high added sugar, provides energy but it is already poor in another nutrients, so that will affect the balance of intake nutrients like mineral, proteins and vitamins.

The increase of consuming sugar leads to several disease especially diabetes type 2, obesity, and cardiovascular disease **(Zaitouni et al., 2018)**.

2-Saccharose

Sucrose is a non reducing disaccharide produced by crystallization from syrups derived from processing sugarcane and sugar beets**(Figure 1).** Sucrose's most important properties are its water solubility and its sweetness. The latter is influenced by temperature, pH, etc **(Colonna et al., 2006)**.

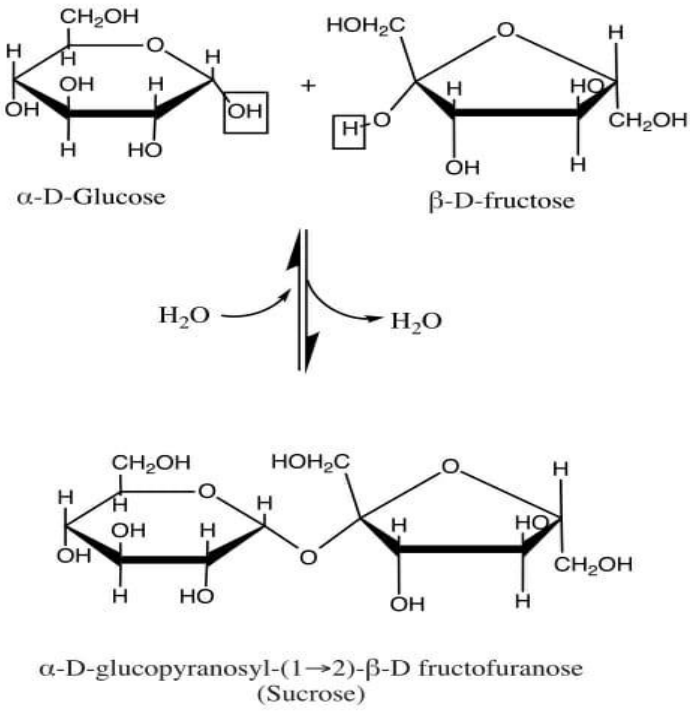


Figure 1. structures of the saccharose (1).

3-Carbohydrates

3.1-Definition

Carbohydrates are the main source of energy that the human body ingests **(Asif et al., 2011)**.Simple carbohydrates or the entire family of carbohydrates can be called sugars in general having the empirical formula CH2O **(Aldairi et al., 2008)**.

A prolonged lack of carbohydrates, the body begins to synthesize glucose from its own proteins, which reduces its protective ability against environmental factors **(Saitkulov et al., 2022)**.

The primary classification of dietary carbohydrate is based on chemistry, that is character of individual monomers, type of linkage (α or β)and degree of polymerization (DP) **(Cummings and Stephen, 2007)**.

3.2-Chemical structure of carbohydrates

Structurally they are poly functional compounds. They contain two types of functional groups-carbonyl and hydroxyl. They may be polyhydroxy aldehydes or polyhydroxy ketones **(Mondal, 2017)**.

Carbohydrates with different ,chemical structures, physical forms ,particle sizes, and fiber contents induce distinct plasma glucose and insulin responses **(Jenkins et al., 1981)**.

The primary classification of dietary carbohydrate is based on chemistry, that is character of individual monomers, type of linkage (α or β) and degree of polymerization (DP) **(Cummings and Stephen, 2007)**.

Carbohydrates chains come in different lengths **(Raven et al., 2014)**.Carbohydrates are classified into mono-saccharides, disaccharides, oligosaccharides, polysaccharides **(Figure2)(Asifetal., 2011)**.Simple carbohydrate refers to monocchacarides and disaccharides, complex carbohydrate refers to polysaccharides such as starch **(Howard and Wylie-Rosett, 2002)**.

A carbohydrate may be termed "complex" if it contains more than one type of monosaccharide building unit **(Seeberger, 2017)**.

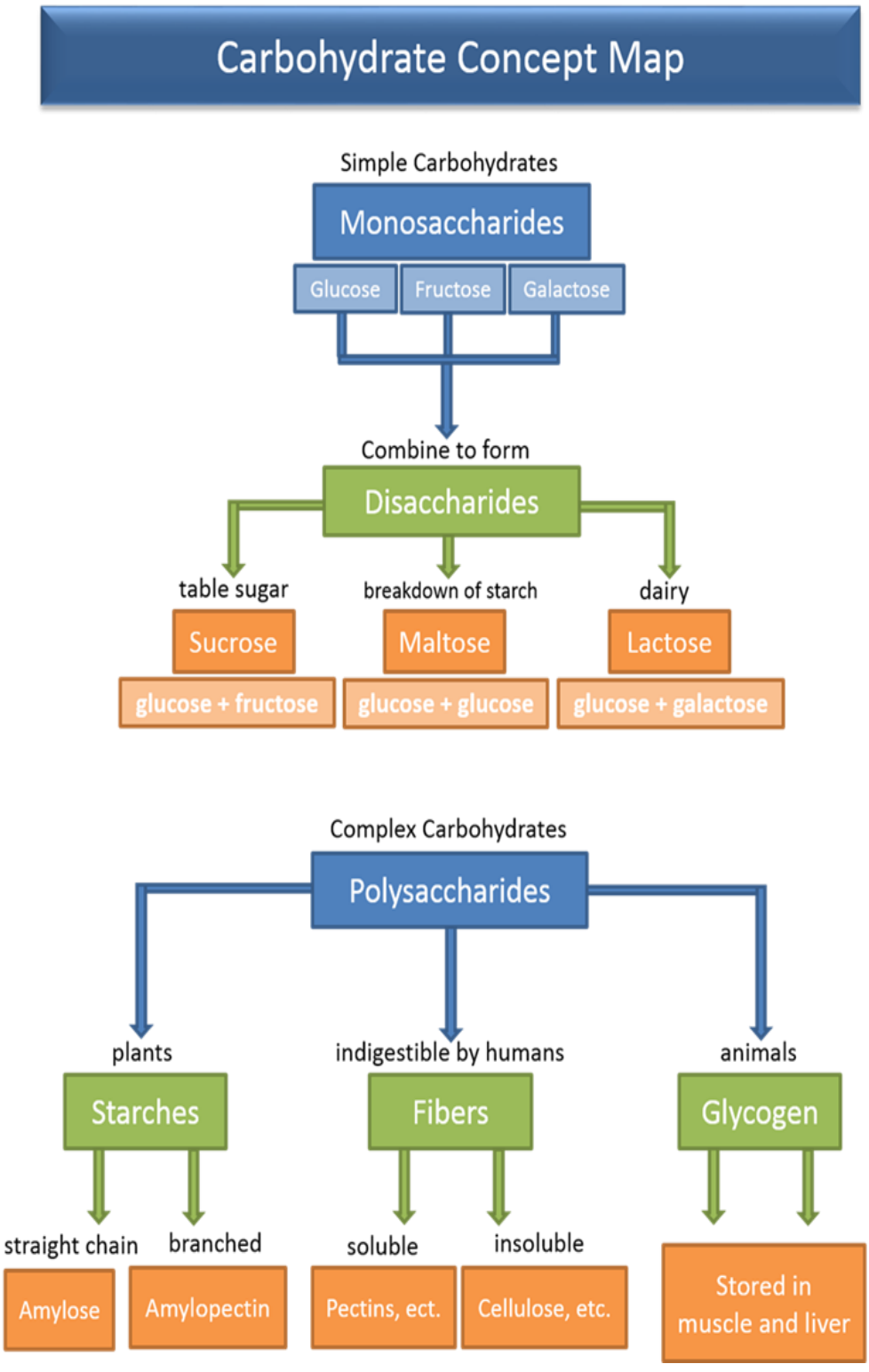


Figure2. Carbohydrate concept map (2).

3.2.1-Monosaccharides

The most common naturally occurring monosaccharide is fructose found in fruits and vegetables **(Howard and Wylie-Rosett, 2002)**.

They are polyhydroxy aldehydes or polyhydroxy ketones which cannot be decomposed by hydrolysis to give simpler carbohydrates. E.g. fructose, Glucose, Galactose etc**...(Figure 3).**

Sugars are also named according to their number of carbons, some of the most common types are trioses (three carbons), pentose (five carbons), and hexoses (six carbons) **(Figure4)(Mondal, 2017)**.

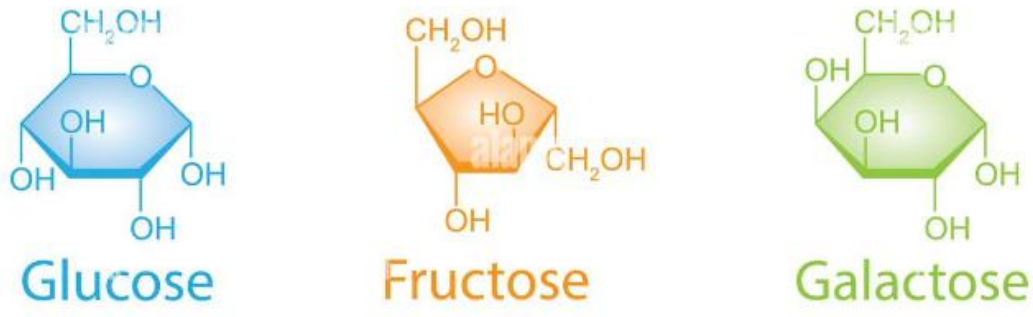


Figure 3. Linear and ring structures of three common monosaccharides. All have the same molecular formula (C6H12O6), but they have different structures (red) and are therefore isomers of each other (3).

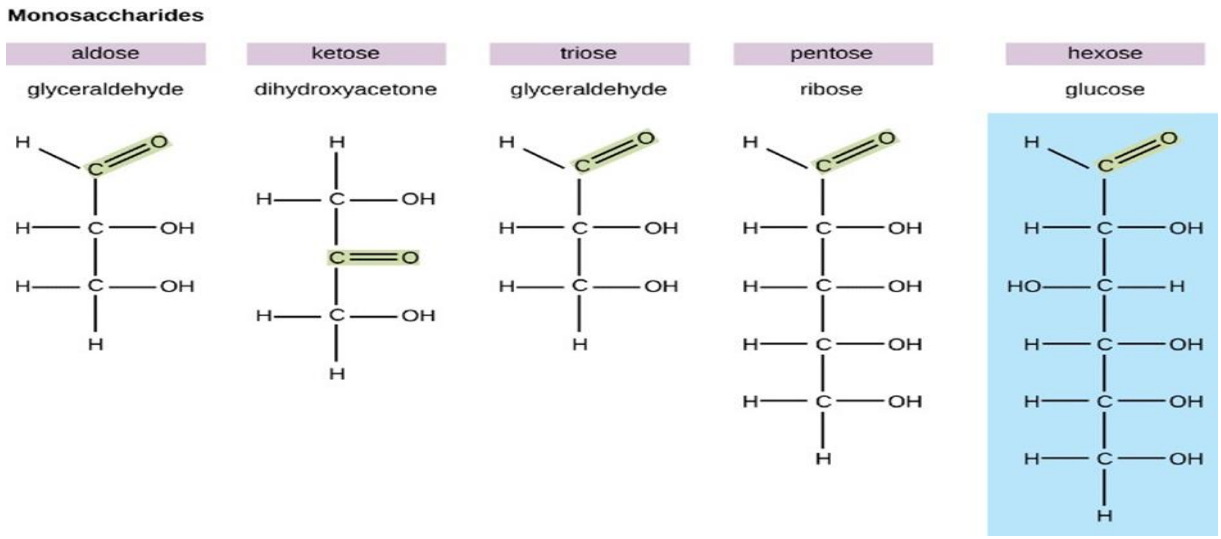


Figure 4. Monosaccharides are classified based on the position of the carbonyl group and the number of carbons in the backbone (4).

3.2.2-Disaccharides

Disaccharides and starch are well known to constitute the major part of the carbohydrates present in our diet **(Dahlqvist and Borgstrom, 1961)**.

Common disaccharides are sucrose, found in sugar cane, sugar beets, honey, and corn syrup; lactose, found in milk products; and maltose, from malt **(Figure 5) (Howard and Wylie-Rosett, 2002)**.

They yield two monosaccharides molecules on hydrolysis. Which have molecular formula is C12H22O11 **(Mondal, 2017)**.

3.2.3-Oligosaccharides

It represent carbohydrates that contain between 3 and 10 single sugar residues and are not relatively abundant in the diet when compared to other more common carbohydrates like those in the disaccharide category . Common oligosaccharides include raffinose , stachynose and verbascose **(Figure6)(Ahnen al., 2020)**.

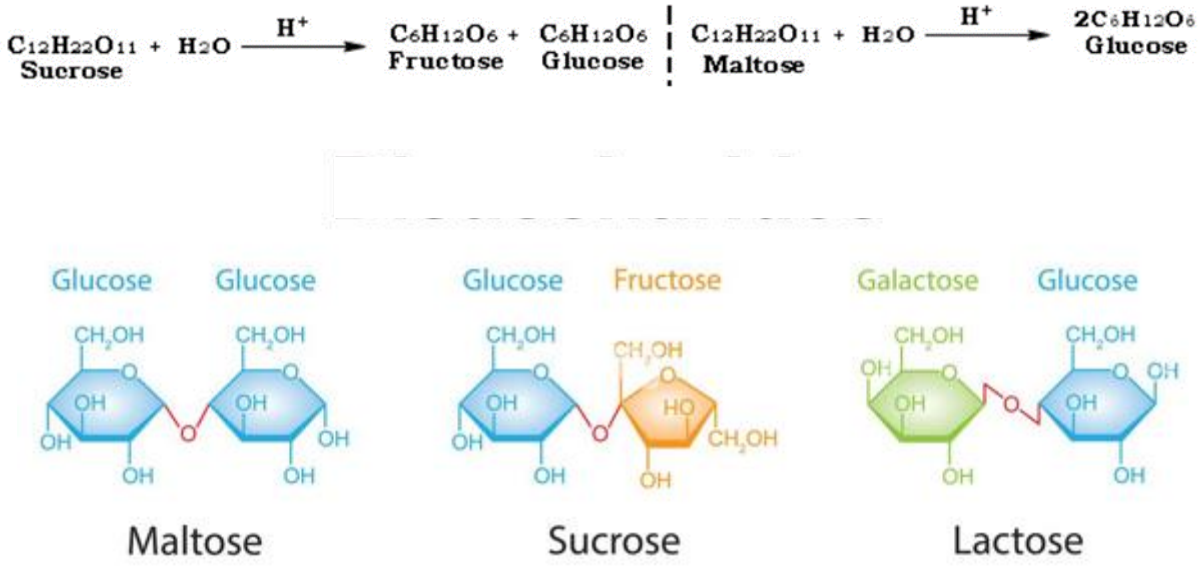


Figure 5. Structures of the three common disaccharides. All contain glucose as one of their subunits; the difference between the three is the second subunit (5).

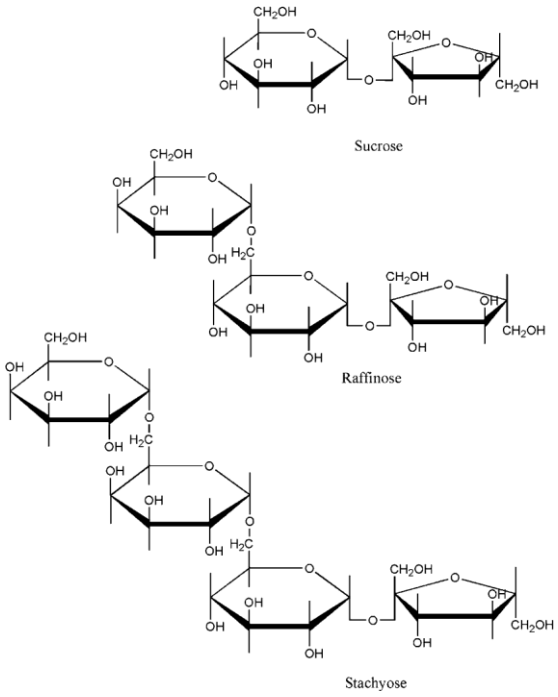


Figure 6. Structures of the three Common oligosaccharides **(Tathiana et al.,2015)**.

3.2.4-Polysaccharides

Polysaccharides are essential macromolecules which almost exist in all living forms **(Mohammed al., 2021)**.It is important component of higher plants, membrane of the animal cell and the cell wall of microbes **(Yu et al., 2017)**.

This term is typically used to denote any linear or branched polymer consisting of monosaccharide residues. the relationship of monosaccharides to polysaccharides is analogous to that of amino acids and proteins, or nucleotides and nucleic acids (polynucleotides) **(Seeberger,2017)**.

They have higher molecular weight, which yield many monosaccharide molecules on hydrolysis. E.g. Starch, Dextrin, Cellulose, glycogen etc…**(Figure7)(Mondal, 2017)**.

4-Uses of sugar

Although the main reason for the use of sugar is its sweet taste, sugar has many other functions in food technology. The most important among these are that added sugar in foods acts as a sweetener, preservative, texture modifier, fermentation substrate, flavouring and colouring agent, bulking agent **(koivistoinen et al., 1985)**.

5-Sugar and inflammation

High sugar intake has long been recognized as a environmental risk factor for increased incidence of many non-communicable diseases, including obesity, cardiovascular disease, metabolic syndrome, and type 2 diabetes.It induce the increase of inflammatory mediators and certain pro-inflammatory cytokines in various tissues, which leads to insulin resistance and low-grade chronic inflammation**(Ma et al., 2022)**.

Fructose is recognized as a major mediator of NAFLD, as a significant correlation between fructose intake and the degree of inflammation and fibrosis**(Muriel et al., 2021)**.

Sugar stimulates the production of free fatty acids in the liver .When the body digests these free fatty acids, The resulting compounds can trigger inflammatory processes .Eating high levels of saturated fats, trans fats, and refined sugar are all risk factors for chronic inflammation **(Marengo, 2019)**.

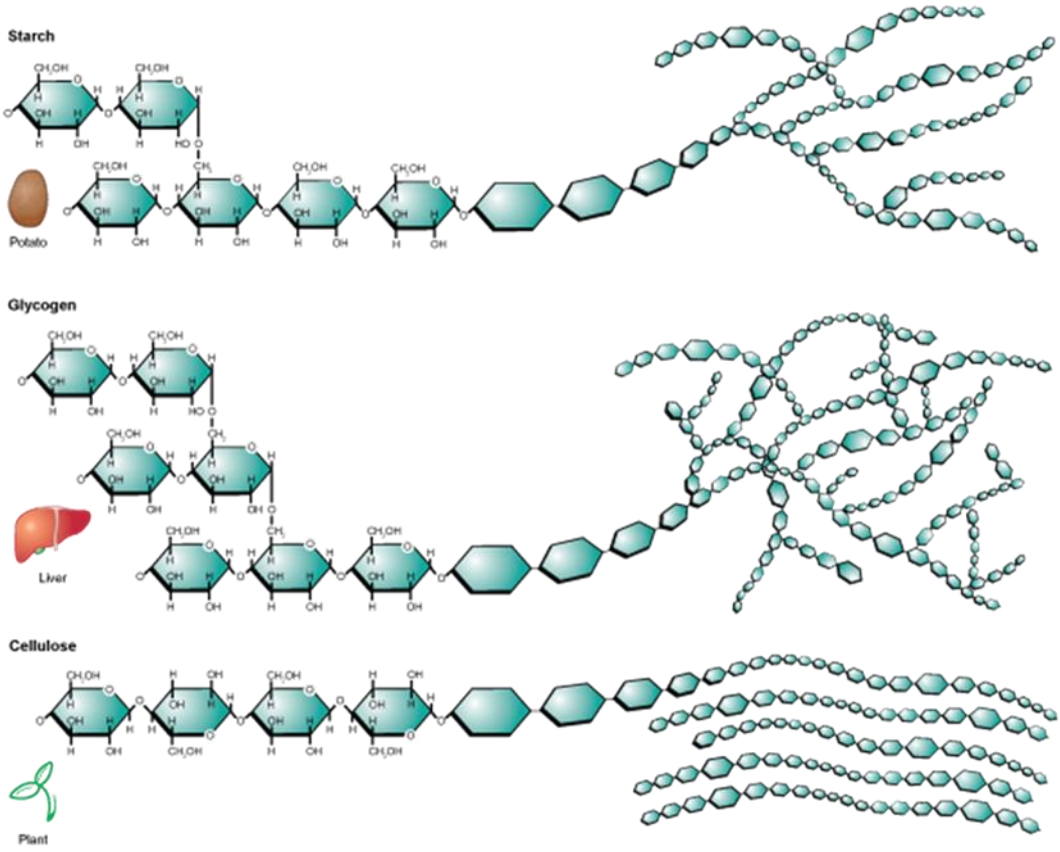


Figure 7. Structures of the three common polysaccharide: starch ,glycogen ,cellulose (6).

Chapter II
Inflammation

II-Inflammation

1-Definition

Inflammation is a complex process, comprising many events, initiated by tissue damage caused by endogenous factors (such as tissue necrosis or bone fracture) as well as exogenous factors. These include various types of damage such as mechanical injury (e.g., cut), physical injury (e.g., burn), chemical injury (e.g., exposure to a corrosive chemical), biological injury (e.g., infection by microorganisms), and immunologic injury (e.g., hypersensitivity reactions) **(Binjamini et al., 1996)**. It is also important for the development of many complex diseases and disorders including autoimmune diseases, metabolic syndrome, neurodegenerative diseases, cancers, and cardiovascular diseases **(Murakami and Hirano, 2012)**.

Inflammation is an evolutionarily conserved physical process, affecting any part of the body in which the immune system senses an infection or injury. The five classic signs of inflammation are redness, heat, swelling, pain, and loss of function **(Figure 8)(Hawiger and Zienkiewicz, 2019)**.

Inflammation represents a fundamental biological process that stands at the foreground of a large number of acute and chronic pathological conditions**(Lugrin et al., 2013)**.

Inflammation involving the innate and adaptive immune systems is known to be the protective immune response for maintaining tissue homeostasis by eliminating harmful stimuli, including damaged cells, irritants, pathogens**(Zhao et al., 2021)**.

2-Stages of inflammation

In response to tissue injury, a multifactorial network of chemical signals initiates and maintains a response designed to treat injured tissue and repair it**(Sherwood and Toliver, 2004**). By stimulating and transporting leukocytes of neutrophils, monocytes, and macrophages directed from the venous system to sites of damage, tissue mast cells also play an important role**(Coussens and Werb, 2002)**.This process includes several stages: In response to tissue injury, a multifactorial network of chemical signals initiates and maintains a response designed to treat injured tissue and repair it**(Sherwood, 2004**). By stimulating and transporting leukocytes of neutrophils, monocytes, and macrophages directed from the venous system to sites of damage, tissue mast cells also play an important role**(Coussens and Werb, 2002)**.This process includes several stages:

2.1-Vasodilatation

The purpose of the vasodilatory response is to facilitate the local delivery of soluble mediators and inflammatory cells. Inflammation induced vasodilatation is mediated primarily by nitric oxide (NO) and vasodilatory prostaglandins**(Sherwood, 2004)**.

Activation of members of the selectine family of adhesion molecules (L-P- and E-selectin) that facilitate rolling along the endothelium of blood vessels.

Release of signals and molecules that activate, stimulate and regulate leukocyte integration by cytokines and inflammatory mediators such as tumor necrosis factor-α (TNF-α) .

Fixation of neutrophils to the vascular endothelial surface by tight adhesion through a4b1 and a4b7 integrins associated with vascular endothelial cell adhesion molecule-1 (VCAM-1) and MadCAM-1**(Coussens and Werb , 2002)**.

2.2-Recruitment of inflammatory cells

Translocation of cells such as neutrophils, monocytes and macrophages through the endothelium to sites of infection by extracellular proteases, such as matrix metalloproteinases (MMPs) **(Coussens and Werb , 2002)** .

A family of chemical cytokines, called chemokines, has the ability to chemically attract specific groups of leukocytes. Activated neutrophils increase their level of Fc receptor expression allowing the increased up take and phagocytosis of pathogens**(Thacker, 2006)**.

2.3-Tissue remodeling and resolution

Resolution occurs after a successful host response. Complete bacterial phagocytosis. Resolving inflammation depends upon apoptosis as well as timely and adequate removal of acute inflammatory cells by macrophages. During apoptosis, neutrophils and eosinophils undergo surface changes enabling phagocytes to recognize and ingest them. The apoptotic process is modulated through extracellular signaling **(Moldoveanu et al., 2022)**.

Tissue remodeling includes tissue metaplasia, granulation, angiogenesis and fibrosis, and roles of prostaglandins (PGs) in these processes have been reported **(Aoki and Narumiya, 2012)**.

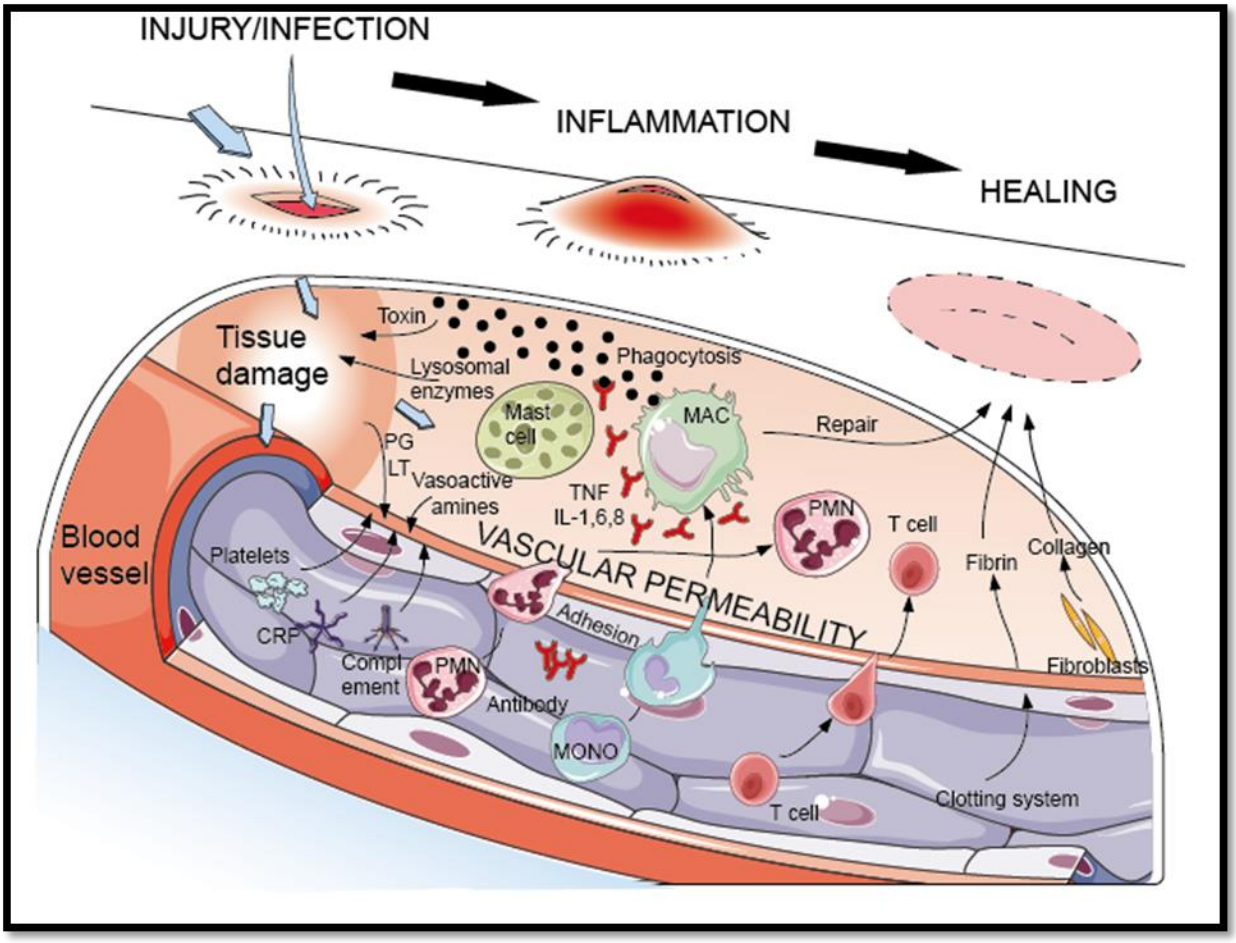


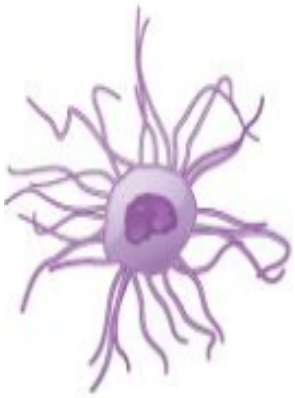
Figure 8. Showing signs of inflammation and the stages of response **(Dimitratos, 2018)**.

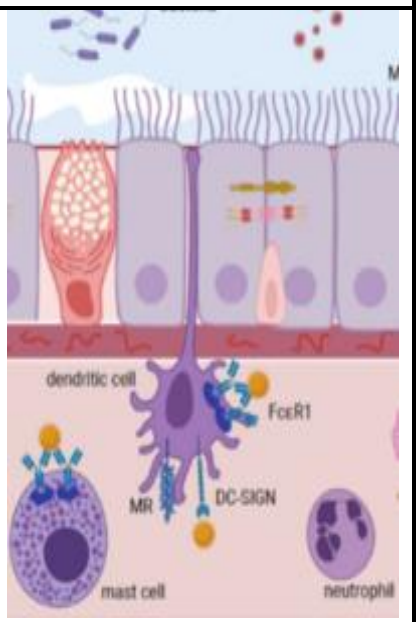
3-Cells of inflammation

The inflammatory response involves a highly coordinated network of many cell types. Activated macrophages, monocytes, and other cells mediate local responses to tissue damage and infection. At sites of tissue injury, damaged epithelial and endothelial cells release factors that trigger the inflammatory cascade, along with chemokines and growth factors, which attract neutrophils and monocytes, and other cells such as lymphocytes (natural killer cells [NK cells], T cells, and B cells), mast cells and dendritic cells.

Table 1: Shows some of the cells involved in inflammation, as well as their functions and structures.

Cells	Functions	cell structures
Mast cells	Participate in the induction and/or propagation of certain inflammatory diseases, through selective release of mediators. Secrete numerous vasoactive and pro-inflammatory mediators such as histamine, serotonin, TNF, kinins and proteases stored in secretory granules **(Theoharis et al., 2012)**. In addition, a number of cytokines (e.g. IL-1, 2, 5, 6, 8, 9, 13, and TNF) and vascular endothelial growth factor (VEGF) are synthesized de novo and released several hours after stimulation **(Mukai et al., 2018)**. It has role in innate or acquired immunity, bacterial infections, as well as in autoimmunity. Super activate T cells through TNF **(Theoharis et al., 2012)**.	
Macrophages cells	**M1:** macrophages are characterized by efficient producers of toxic effector molecules (ROS and NO) and inflammatory cytokines (IL-1β, TNF, IL-6); participate as inducers and effector cells in polarized Th1 responses. **M2:** repond to stimuli (IL-4 and IL-13;	

	alternative inflammation) and (immune complexes, FcγR/TLR triggering),and (IL-10, TGF-β, glucocorticoids; deactivation) .take part in polarized Th2 responses, allergy, parasites clearance, dampening of inflammation, tissue remodeling, angiogenesis , immunoregulation**(Italiani and Boraschi, 2014)**.	
Dendritic cells	It is a part of the innate immune system in to sense and respond to external pathogenic stimuli via PRRs such as TLRs. and secretion of type I interferons. migration to specific destinations , and the release of cytokines and chemokines **(Szabo et al., 2018)**. This migration depends on CCR7 from peripheral tissues to lymphoid tissues for host defense against pathogens and immune tolerance of harmless self- or non self-antigens**(Liu et al., 2021)**.	
Monocyte cells	Have the ability to differentiate into monocyte-derived macrophages, and thus It has the ability to phagocytosis and antigen presentation, innate response/immune responses and migration, secretion of cytokines, secretion of TNF-α, IL-1β, IL-6 and CCL3 upon TLR stimulation and regulation of apoptosis, differentiation **(Kapellos et al., 2019)**.	

Neutrophils cells	The role of neutrophils is phagocytosis, degranulation, and the release of nuclear material in the form of neutrophil extracellular traps (NETs). Respond to multiple signals by producing several cytokines and other inflammatory factors that influence and regulate inflammation and also the immune system such as IL-1α,IL-1β,IL-6,IL-10, and TNF-α**(Rosales,2018)(Wright et al., 2010)**. TANs are pro inflammatory and anti tumorigenic.	
Epithelial cells	Epithelial cells derived from airway, intestinal and ocular mucosal sites actively participate during inflammatory processes. They express adhesion and co-stimulatory molecules in response to different cytokines and/or chemokines, and they also secrete several cytokines/chemokines that contribute to inflammation. Can play roles as non-professional antigen presenting cells in the recruitment and activation of lymphoid cells **(Enríquez et al., 2008)**.	

4-Types of inflammation

Inflammation can be divided into two categories according to the duration of the disease: acute and chronic inflammation.

4.1-Acute inflammation

Tissue damage due to trauma, microbial invasion, or noxious compounds can induce acute inflammation. It starts rapidly, becomes severe in a short time and symptoms may last for a few days for example cellulitis or acute pneumonia. Sub acute inflammation is the period between acute and chronic inflammation and may last 2 to 6 weeks **(Pahwa et al., 2022)**.

The prototypical acute inflammatory response, characterized by local vasodilation, extravasation of leukocytes, and release of multiple plasma components, has been particularly well worked up in the field of invasion by microorganisms. Activation of an acute inflammatory response is a fundamental requirement to eradicate threats to the host organism such as bacterial or viral infections **(Feehan and Gilroy, 2019)** and these processes are mediated largely by the detection of so-called pathogen-associated molecular patterns (PAMPs) **(Erridge, 2008)**.

Initiation of inflammation, is mediated by resident immune cells via pathogen recognition receptors (PRRs) such as Toll-like receptors (TLRs), leading to the synthesis of soluble mediators such as pro-inflammatory cytokines, which activate downstream pro-inflammatory signaling **(Feehan and Gilroy, 2019)**.

4.2-Chronic inflammation

Chronic inflammation is a risk factor for a broad diseases such as hypertension, diabetes, atherosclerosis, and cancer **(Sanada et al.,2018)**.

Chronic inflammation is characterized by the simultaneous occurrence of destruction and healing of tissues **(Zhao al., 2021)**.

The main infiltrating immune cells in chronic inflammation sites are macrophages and lymphocytes**(Moldoveanu et al., 2022)**.If the pro-inflammatory stimulus is not eliminated during the acute inflammation process**(Zhaol et al., 2021)**, characterised by high plasma levels of numerous pro-inflammatory cytokines IL-1β, IL-6, TNF-α and CRP**(Rehman and Akach, 2016)**. It will lead to chronic inflammation, autoimmunity, tissue fibrosis, and necrosis. The

persistence of inflammatory factors and damage to tissues are the key factors of chronic inflammation **(Zhao et al., 2021)**.

The underlying purpose of chronic inflammation is to clear necrotic debris produced during the acute inflammatory process, to provide defense against persistent infections, and to heal and repair the damage. Destruction of the normal tissue architecture results in scarring**(Thacker, 2006)**.

5-Markers of Inflammation

Markers of inflammation are used to detect acute inflammation that might indicate a specific disease and also to assess treatment response. Raised levels of inflammatory markers can indicate the probability of infections, autoimmune conditions, and cancers. Where levels are normal, certain conditions can be ruled out. Although they are valuable for indicating diseases, inflammatory markers are not specific enough to allow diagnosis of serious underlying disease **(Watson and Hamilton, 2012)**.

The most common inflammatory markers are C-reactive protein, erythrocyte sedimentation rate, and pro-calcitonin. Although other markers of inflammation are useful in certain circumstances **(Table 2)**.

Table 2: Inflammatory markers.

Marker	Application
C-reactive protein (CRP)	It is a biological mark, used as an early indicator to detect infections, tissue injury or acute infection at an early stage**(Boncler et al., 2019)**.
Erythrocyte sedimentation rate (ESR)	Is a common hematology test that may indicate and monitor an increase in inflammatory activity within the body caused by one or more conditions such as autoimmune disease, infections or tumors, and determine the presence of increased inflammatory activity and pulmonary tuberculosis **(Bull et al., 1993)(Bray et al., 2016)**.
Procalcitonin (PCT)	Marker of bacterial infection, severe viral infection, pancreatitis, tissue trauma, and certain autoimmune disorders. Useful in the diagnosis of sepsis **(Meisner, 2014)**.

Marker	Application
Serum amyloid A	Acute phase protein released in response to inflammation or infection. Concentration increases dramatically during acute infection and injury **(Targońska and Majdan, 2014)**.
Cytokines	Small proteins including interleukins, chemokines, interferons, and tumor necrosis factors with varying roles in inflammation and immunity. They are released in a number of paracrine, autocrine, or endocrine pathways and have been implicated in a variety of infections and immune system-affecting disorders by both proinflammatory and anti-inflammatory mechanisms. Cytokines which have proinflammatory effects include interferon IFNγ, interleukin IL-17, IL-1β, and tumor necrosis factor TNFα, and those with anti-inflammatory effects include IL-10, IL-4, and IL-1**(Monastero and Pentyala, 2017)**.
Alpha-1-acid glycoprotein	AGP glycoforms are very useful in the detection of intercurrent infections in the course of rheumatoid arthritis, systemic lupus erythematosus, or myelo blastic leukaemia, and in the detection of secondary infections in human immunodeficiency virus infected individuals and differentiation between various forms of trophoblastic disease **(Mackiewicz and Mackiewicz, 1995)**.
Plasma viscosity	The plasma viscosity is rising in the presence of proteins produced in reponse to infection or inflammation (erythrocyte sedimentation rate, C-reactive protein, and platelet)**(Lobo et al., 1992)**.
Ceruloplasmin	One of the main proteins in metabolism and distribution of copper in blood serum, and appears to act as an antioxidant. Positive-phase protein, meaning that its level changes in acute and chronic inflammation **(Adamczyk et al., 2016)**.
Hepcidin	Regulator of iron metabolism produced by the liver. Iron deficiency can be indicated by reduced hepcidin levels. Levels of hepcidin are often abnormally high during inflammation, such as during sepsis or in patients with IBD**(Angelo,**

Marker	Application
	2013).
Haptoglobin	Acute phase protein induced by inflammation, which can bind hemoglobin and act as an antioxidant**(Wang et al., 2001)**.

Chapter III

C-reactive protein

III-C-reactive protein

1-Definition

C-reactive protein (CRP) is a homo-pentameric classical acute phase inflammatory protein. In 1930, it was initially discovered by Tillet and Francis during the investigation of the sera of patients suffering from the acute condition of Pneumococcus infection. It was then named for its reaction capacity (for precipitation) with the bacterial cell wall somatic capsular (C)-polysaccharide of Streptococcus pneumonia **(Figure9) (Tillet et al., 1930)**.

CRP is a highly sensitive marker of inflammation and tissue damage, and levels can rise to more than 500 mg/liter in a variety of acute or chronic inflammatory conditions **(Tall, 2004)**. It is a major acute phase protein whose concentration may increase more than 1,000-fold in severe inflammatory states **(Pathak and Agrawal, 2019)**.

CRP is synthesized primarily in liver hepatocytes but also by smooth muscle cells, macrophages, endothelial cells, lymphocytes, and adipocytes **(Sproston and Ashworth, 2018)**.

It is one of the most important proteins that is rapidly produced during an acute-phase response upon stimulation by IL-6, TNF-α, and IL-1-β originating at the site of inflammation or pathology **(Severine et al., 2004)**.

Reported that CRP has both pro-inflammatory and anti-inflammatory properties. It plays a role in the recognition and clearance of foreign pathogens and damaged cells by binding to phosphocholine, phospholipids, histone, chromatin, and fibronectine**(Nehring et al.,2017)**.

2-Structure of C-reactive protein

Human CRP (hs CRP) is a pentameric protein composed of five identical non-covalently bound subunits of 206 amino acid residues with a molecular weight of ~23 kDa. CRP binds to phosphocholine (PCh) in a Ca2+-dependent manner.It exhibits immunological cross-reactivity with human CRP **(Figure 9)(Pathak and Agrawal, 2019)**.The calcium ions are important for the stability and binding of ligands **(Sproston and Ashworth, 2018)**.

Other ligands include histones, chromatin, and small nuclear ribo-nucleoproteins**(Vermeire et al., 2004)**.

Each protomer has been found by x-ray crystallography to be folded into two antiparallel sheets with a flattened jellyroll topology similar to that of lectins such as concanavalin A. Each

protomer has a recognition face with a phosphocholine binding site consisting of two coordinated calcium ions adjacent to a hydrophobic pocket **(Thompson et al., 1999)**.

The loss of the pentameric structure of CRP results in modified or monomeric CRP (mCRP), which is a naturally occurring form of CRP and it is a tissue-based rather than a serum based molecule. mCRP is less soluble than CRP and tends to aggregate **(Figure 10)(Shrivastava et al., 2014)**.

Pentameric C-reactive protein (pCRP) can undergo protomer dissociation into mCRP in the absence of Ca2+ or upon binding to lysophosphatidyl-choline monolayers or altered cell membranes. Or on the surface of activated platelets and apoptotic monocytic THP-1 cells **(Wu et al., 2015)**.

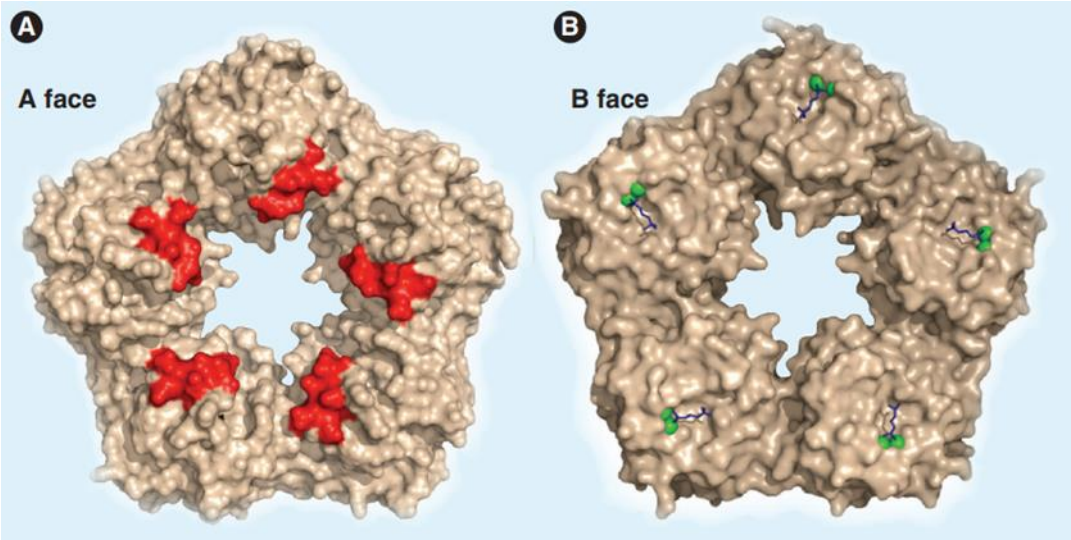


Figure 9. Pentameric structure of C-reactive protein (CRP). (A) Space - filling model of the A face (receptor and C1q binding) of the CRP pentamer with the ridge helix in red. (B) Spacefilling model of the CRP molecule showing a phosphocholine molecule (blue) with the two calcium molecules (green) located in the binding site of each protomer on the B face (ligand - binding face) **(Peisajovich et al., 2008)**.

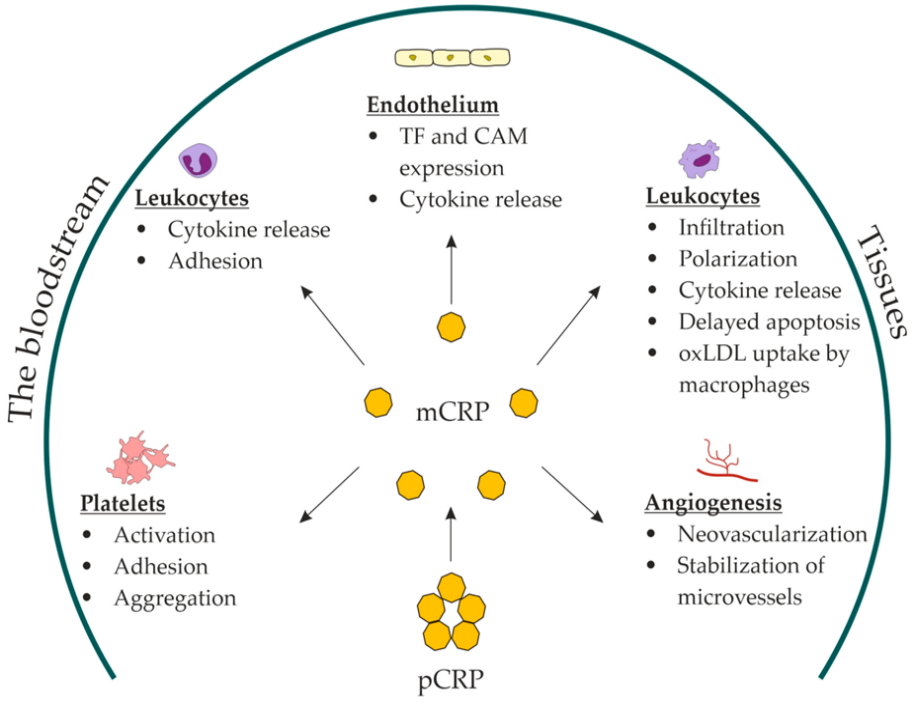


Figure 10. Proposed roles for mCRP in atherosclerosis. mCRP, monomeric C-reactive protein; pCRP: pentameric C-reactive protein. TF: tissue factor. CAM: cell-adhesion molecules. oxLDL: oxidized low-density lipoproteins **(Melnikovet al., 2023)**.

3-The role of C-reactive protein

The main biologic function of CRP is determined by its ability to recognize pathogens and damaged cells of the host and to mediate their elimination by recruiting the complement system and phagocytic cells **(Volanakis, 2001)**.

It is directly amplifies and facilitates innate immunity, it increases LDL uptake into macrophages and enhances the ability of macrophages to form foam cells. It also binds the phosphor-choline of oxidized LDL. CRP activates macrophages to secrete tissue factor, a powerful procoagulant, which can lead to disseminated intravascular coagulation and ultimately to thrombosis during inflammatory states **(Shrivastava et al., 2014)**.

CRP up regulates the expression of adhesion molecules in endothelial cells (ECs) that can attract monocytes to the site of injury **(Pfutzner et al., 2010)**.

reported that CRP increases plasminogen activator inhibitor-1(PAI-1) expression and activity. PAI-1 is a protease inhibitor that regulates fibrinolysis by inhibiting tissue plasminogen activator. Increased PAI-1 indicates lowered fibrinolysis and thus leads to atherogenesis**(Davis et al.,2012)**.

CRP also indirectly affects specific immune response, during atherogenesis, through the increase of IL-12 production from macrophages, with the subsequent induction of CD4 + T lymphocytes differentiation and Interferon gamma production **(Calabro et al., 2012)**.

hs-CRP correlates with extent of atherosclerosis, and high triglyceride and BMI is closely associated with high hs-CRP levels in patients with dyslipidemia **(Swastini et al., 2019)**.

4-Methods for measuring C-reactive protein

Initially, high-sensitivity quantification methods were based on ELISA, utilized in several population studies despite its cumbersome routine use in clinical laboratories. As a consequence, more accessible methods, such as immune nephelo metric techniques and, more recently, automatized immune luminometry and immune turbidimetry, have been implemented, improving the sensitivity of the quantification even in cases of very low concentrations. Additionally, these are inexpensive techniques, an important aspect regarding its routine use in clinical practice **(Salazar et al., 2014)**.

5-C-reactive protein and inflammation

The main role of CRP in inflammation tends to focus around the activation of the C1q molecule in the complement pathway leading to the opsonization of pathogens **(Sproston and Ashworth, 2018)**. It can also initiate cell-mediated pathways by activating complement as well as to binding to Fc receptors of IgG **(Figure 11)(Pradhan et al., 2001)**.

pCRP induces the up regulation of cell adhesion molecules such as intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and E-selectin via NF-κB up regulation**(Thiele et al., 2015)**.

CRP binds to Fc receptors with the resulting interaction leading to the release of pro-inflammatory cytokines **(Du, 2000)**.

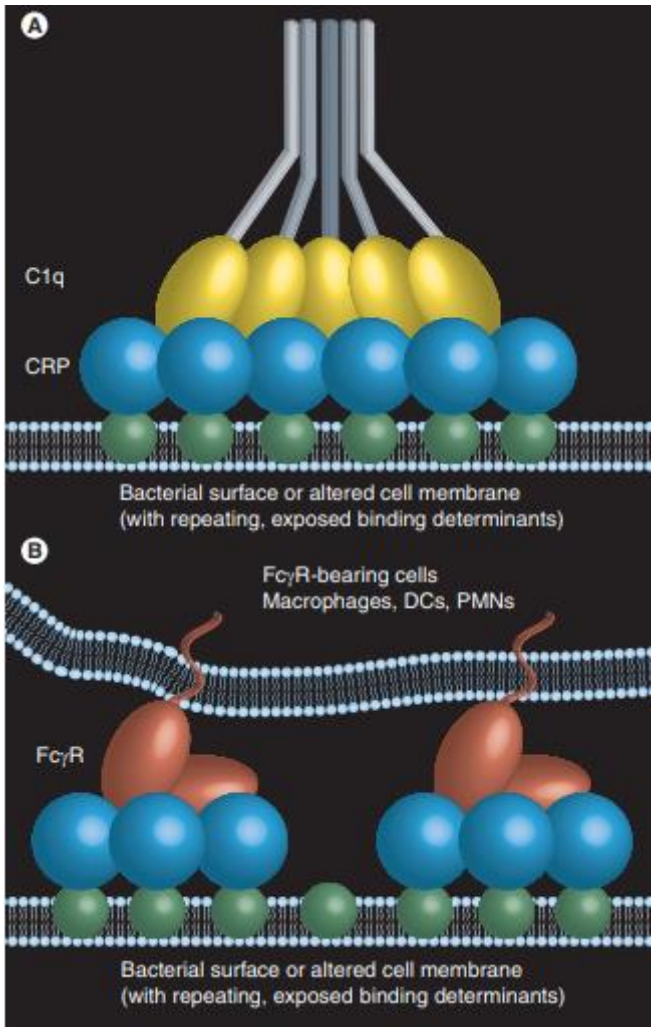


Figure 11.CRP bound to bacterial or altered cell surfaces. CRP binds to a surface on its B-face phosphocholine-binding site, leaving the A face exposed. This allows each pentamer to bind either (A) one of the six globular heads of C1q leading to the activation of the classical complement cascade or; (B) Fcγ R on the surface of macrophages, DCs or PMNs. The type of Fcγ R helps to determine the downstream effect of this binding. CRP: C-reactive protein; DC: Dendritic cell; Fcγ R: Fcγ receptor; PMN: Polymorphonuclear cell (neutrophil) **(Peisajovich et al., 2008)**.

Chapter IV

Atherosclerosis

IV- Atherosclerosis

1-Definition

The term atherosclerosis of Greek origin, meaning thickening of the intimal layer of arteries and accumulation of fat. Fatty material is located in the central core of the plaque, covered by fibrous cap. The term, atherosclerosis consists of two parts; atherosis (accumulation of fat accompanied by several macrophages) and sclerosis (fibrosis layer comprising smooth muscle cells [SMC], leukocyte, and connective tissue**.(Rafieian et al., 2014).**

Atherosclerosis is a chronic, inflammatory disease of the arterial wall that underlies many of the common causes of cardio-vascular morbidity and mortality, including myocardial infarction (MI), and cerebro-vascular and peripheral vascular disease. Early pathological descriptions view edatherosclerosis as an end-stage degenerative process that inevitably resulted in a generalized narrowing of the arterial lumen. However, progress in our understanding of the pathophysiology and the underlying cellular and molecular mechanisms has revealed that atherosclerosis is a dynamic biological process**(Figure 12)(Douglas and Chanon, 2014).**

The lesions result from an excessive, inflammatory-fibro proliferative response to various forms of insult to the endothelium and smooth muscle of the artery wall. A large number of growth factors, cytokines and vasoregulatory molecules participate in this process. Our ability to control the expression of genes encoding these molecules and to target specific cell types provides opportunities to develop new diagnostic and therapeutic agents to induce the regression of the lesions and, possibly, to prevent their formation**(Ross,1993).**

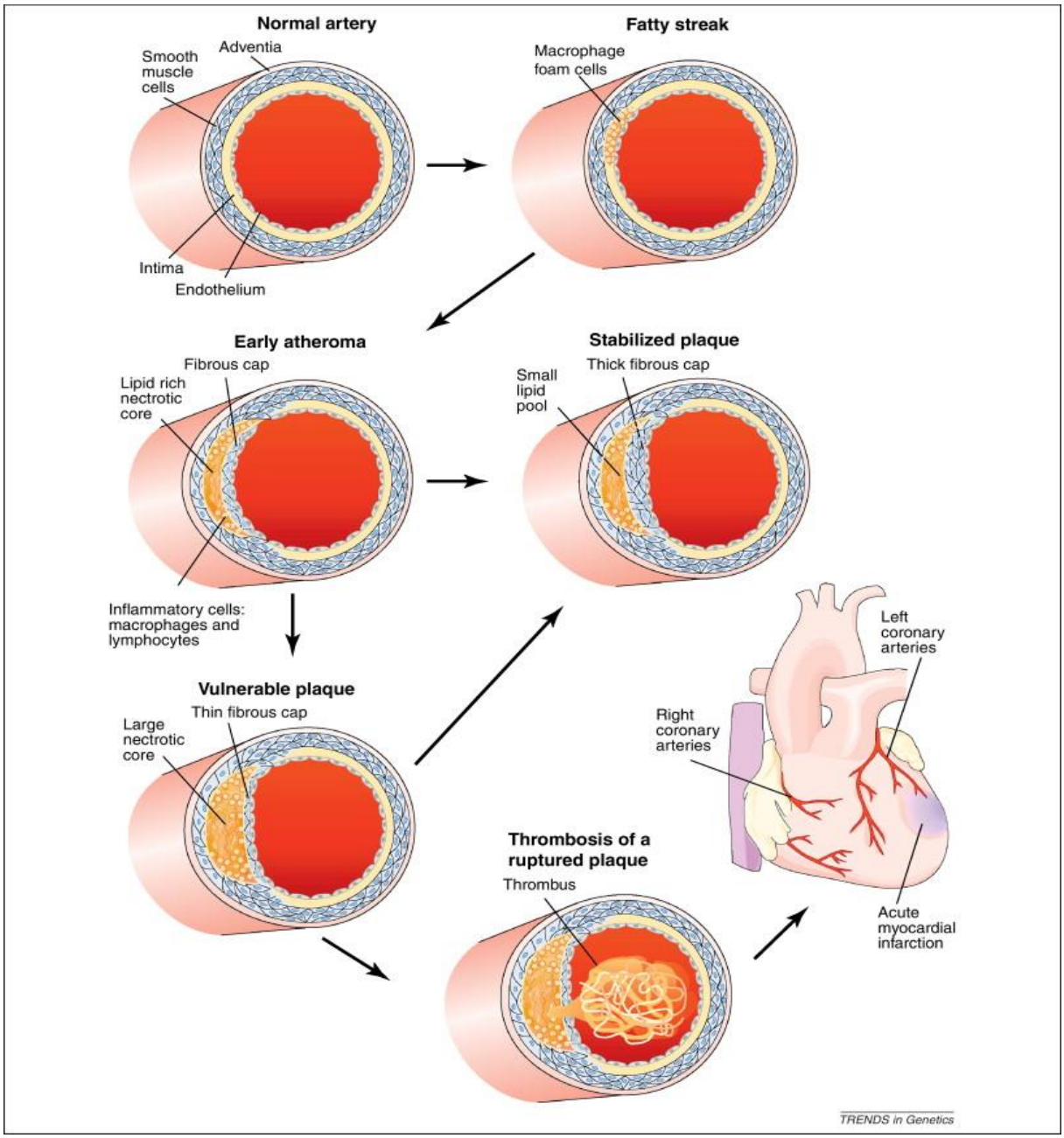


Figure 12 . Genetics of atherosclerosis(7).

2-Causes of atherosclerosis

Development of atherosclerotic lesions probably requires low-density lipoprotein a particle that carries cholesterol through the blood **(Figure13**).

Other risk factors for atherosclerosis and its thrombotic complications include hypertension, cigarette smoking and diabetes mellitus. Increasing evidence also points to a role of the immune system, as emerging risk factors include inflammation and clonal haematopoiesis**(Libby et al., 2019)**

Obesity, and in particular abdominal obesity, is associated with insulin resistance and atherosclerotic disease. An increase in the visceral adipose tissue (VAT) compartment, as seen in abdominal adiposity, is accompanied by an increase in adipocyte size and adipose tissue dysfunction, resulting in augmented gene expression of inflammatory cytokines in adipocytes, infiltration of adipose tissue by macrophages and production of inflammatory cytokines by adipose tissue macrophages **(Verhagen and Vissern,2011).**

Atherosclerosis Common forms of coronary artery disease result from the combination of genetic susceptibility and an unhealthy environment.

Rare mendelian forms, such as familial hypercholesterolemia and Tangier disease, have provided important insights into the disease. Studies of candidate genes associated with predisposing conditions, such as hyperlipidemia, low HDL levels, diabetes, hypertension, and pro-coagulant disorders, have revealed a number of genes with significant or suggestive association or linkage with traits relevant to atherosclerosis **(Araùjo and lusis,2004).**

Experimental studies and many clinical observations have shown that hyperlipidemia is essential but not sufficient to produce atherosclerosis unless there is inflammation as well. Inflammation was, in fact, implicated in atherosclerosis by Virchow as far back as in 1858 .Many cytokines and chemokines are involved in the development and progression of the atherosclerotic plaque **(Shah and Lecis,2019).**

The key cell types involved in atherosclerosis include endothelial cells, monocytes/macrophages, smooth muscle cells, lymphocytes and platelets. Several hundred gene products have been targeted as potential candidates in the analysis of the genetic component of atherosclerosis **(Hegele,1996).**

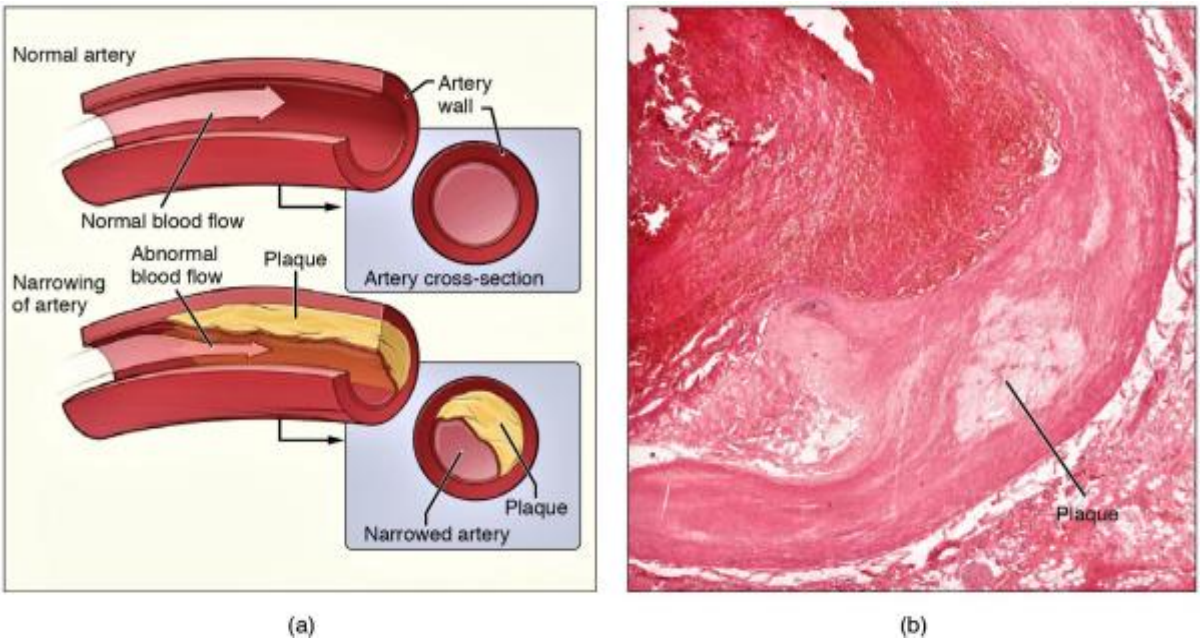


Figure13. Different stages in progression of atherosclerosis (8).

3-Steps of atherosclerotic plaque

Atherosclerosis has several stages of information and progression of plaque which are briefly described in the following:

3.1-Fatty streak development

This may start in early life like in the 20s itself. This is an initial step of plaque formation where LDLs enter middle layer and undergo accumulation when their amount increases in blood the noxidize to pro-inflammatory cells. Due to this accumulation, the inflammatory mediators activated and secrete VSMC that attracts monocytes, lymphocytes, mast cells, neutrophils, proteoglycans, collagen, elastic fibers.

Monocytes in intima get developed into foam cells via macrophage formation.

This lipid deposition is considered as the first stage and can be treated based on the amount of accumulation of lipids **(Reddy, 2020).**

3.2-Fibroatheroma formation

It is observed in late teens. In this step the foam cells and inflammatory cells play a key role in the progression of a theroma. Proteoglycans that are secreted from extra cellular matrix increases the lipid-binding capacity. In this process, few cells may die and these dead cells

progress the inflammation. All the dead cells are accumulated and covered by a lipid-rich core which occupies about 50% of arteries diameter leading to obstruction.

3.3-Thin-cap fibro atheroma and rupture

This is seen in persons above 50 yrs. A thin cap develops over the plaque. In some areas the cap becomes thin and may rupture leading to thrombo genesis which is a life-threatening risk. This occurs mainly in the cardiovascular system leading to many diseases. The ruptured caps some times heal and involve again the accumulation of collage leading progression of atheromatous plaque**(Figure 14)(Reddy, 2020).**

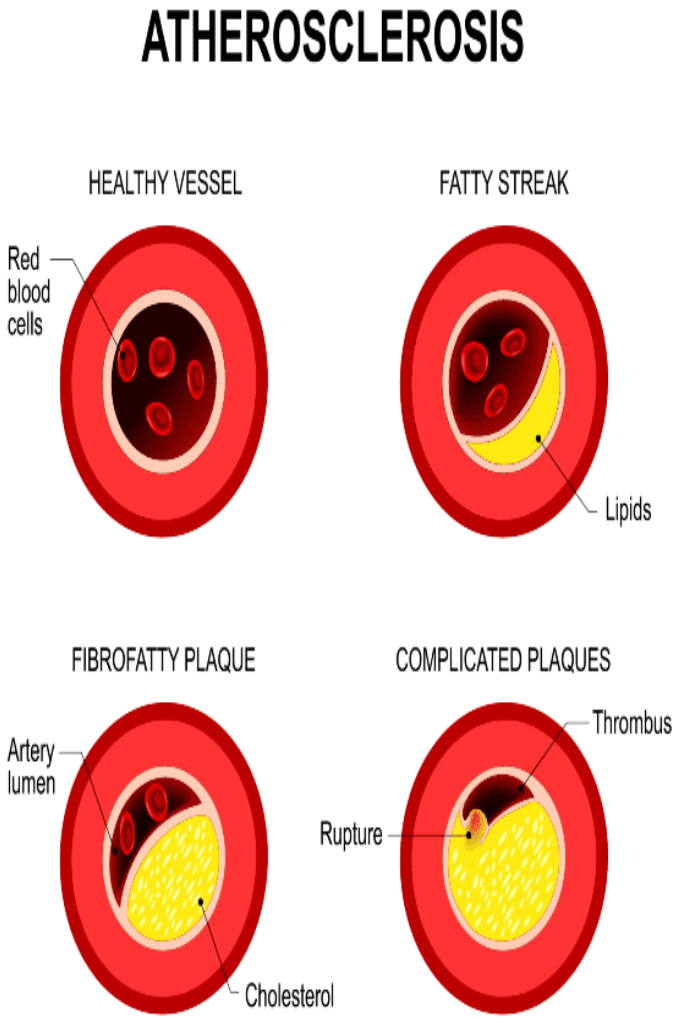


Figure 14 . Stages of atherosclerosis (9)**.**

4-Risk factor

In the past several years, evidence has accumulated that factors other than conventional risk factors may contribute to the development of atherosclerosis. Conventional risk factors predict less than one half of future cardio-vascular events. Furthermore, conventional risk factors may not have the same causal effect in different ethnic groups in whom novel risk factors may have a role. These newer risk factors for atherosclerosis include homocysteine, fibrinogen, impaired fibrinolysis, hyper-coagulability, lipoprotein, small dense low-density lipoprotein-cholesterol, and inflammatory-infectious markers. Identification of other markers associated with an increased risk of atherosclerotic vascular disease may allow better insight into the pathobiology of atherosclerosis and facilitate the development of preventive and therapeutic measures **(Kullo et al.,2000).**

Ideally, the information derived from newer molecular approaches to define the etiology of atherosclerosis could be integrated into evidence-based practice strategies in order to enhance health care delivery to subjects at high risk **(Hegele,1996).**

4.1-Endothelial dysfunction

Normal endothelium functions in an inhibitory mode; it inhibits smooth muscle contraction, plate let aggregation, vascular smooth muscle growth, thrombosis, and white cell (e.g., monocyte) adhesion, which is an early abnormality in the generation of an atherosclerotic plaque. Indeed, atherosclerosis is likely a consequence of endothelial dysfunction. Understanding the role of the endothelium in vascular tone has provided new insights into the evaluation of atherosclerosis and its consequences in patients **(Glasser et al ., 1996).**

4.2-Hypertension

Hypertension is an independent indicator of increased risk of coronary events. Reduced endothelium-derived relaxing factor occurs in hypertensive patients with left ventricular hypertrophy. These patients can develop large and small vessel vasoconstriction, reduced nutrient blood flow, and myocardial ischemia **(Glasser et al ., 1996).**

4.3-Menopause

The lower frequency of coronary atherosclerosis in premenopausal women has been associated with the protective effects of estrogen. Further, epidemiologic studies have suggested a protective effect of hormone replacement therapy in postmenopausal women .This protective effectis not likely to result solely from the favorable lipid alterations associated with hormone replacement **(Glasser et al ., 1996).**

Several studies have demonstrated that estrogens can improve the endothelium dependent relaxation of atherosclerotic coronary arteries in ovary ectomized female monkeys **(Glasser et al ., 1996).**

4.4-Diabetes mellitus

The mechanisms for the development of vascular disease in diabetes are poorly understood. Cohen has reviewed studies of endothelial dysfunction in diabetic patients and animals and studies of the effect of exposing normal blood vessels and cultured endothelial cells to elevated concentrations of glucose**(Glasser et al .,1996).**

Chapter V

Anatomy of the aorta

V-Anatomy of the aorta

1- Heart

The heart is a four-chambered pump, consisting of two pumps arranged in series. one pump (the right heart) drives blood through the lungs (the pulmonary circulation) and then back to the heart, while the other pump (the left heart) drives the oxygenated blood around the body (the systemic circulation). Coordination of the mechanical activity of the heart is provided by an electrical signal **(Figure 15) (keener and Sneyd, 2009).**

The heart is a specialised pump that functions by regular and continuous contractions for delivery of blood throughout the body. The pumping action is caused by a flow of electricity through the heart that repeats itself in a cycle, known as heart rate (HR) or heart pulse. HR is the speed of the heartbeat measured by the number of contractions per unit of time, a measure determined by calculating the heart rate variability (HRV) from electrocardiogram (ECG) **(Dong ,2016).**

The existence of the heart well known to the ancient GREEKS ,who gave it the name *kardia* ,as in cardiac ,tachycardia , and bradycardia . Aristotle thought that the heart was the seat of the soul and the center of man .

GALEN, the father of experimental physiology .knew that the heart set the blood in motion .He discovered that arteries contain blood and not air **(Opie, 2002).**

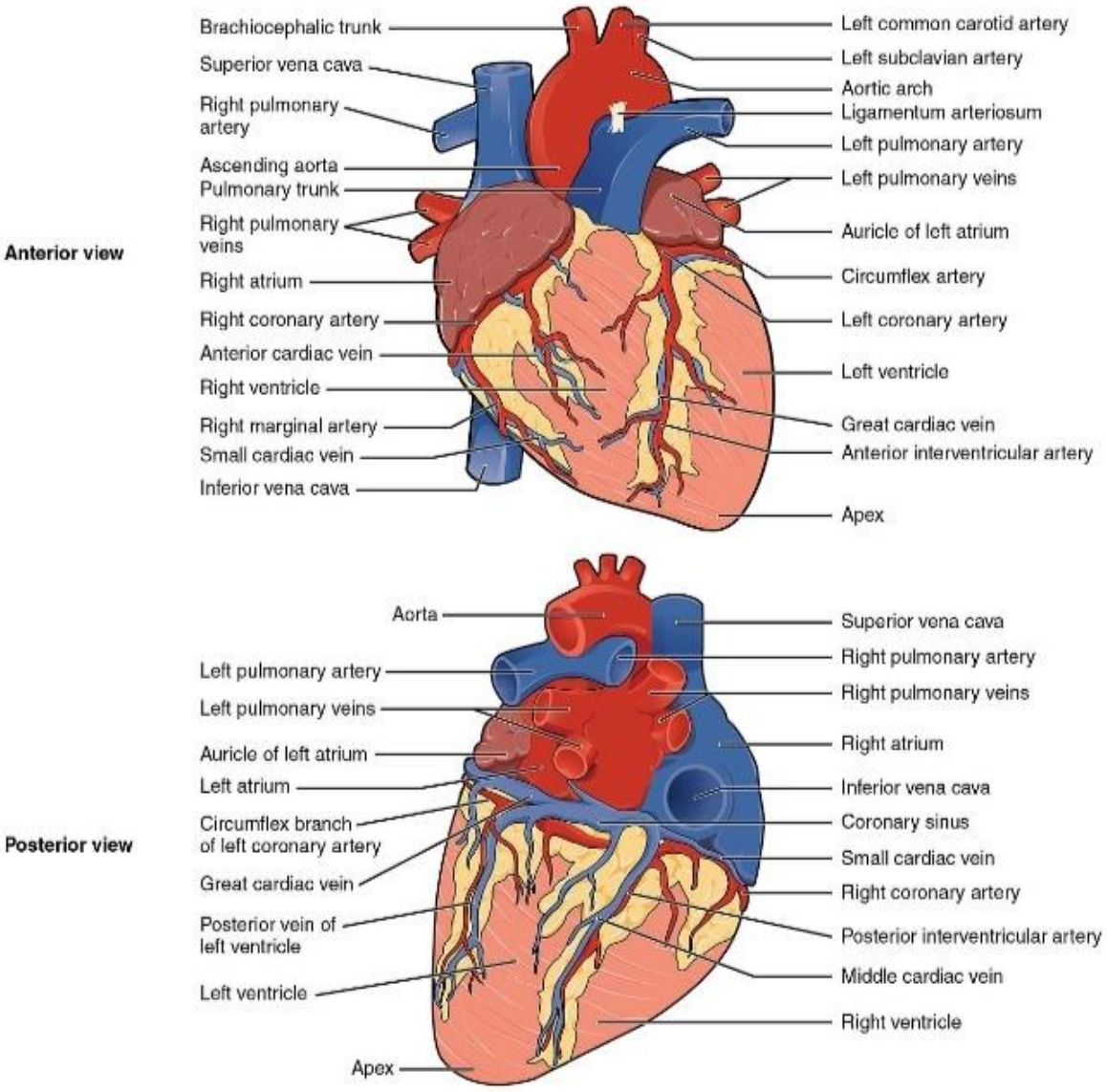


Figure 15. Anatomy of the heart (10).

2-Arteries of the thoracic cavity

The arch of the aorta has three major branches: the brachiocephalic trunk, left common carotid artery, and left subclavian artery. After the aortic arch, the aorta begins its descent, becoming the thoracic aorta at the level of the sternal angle and the abdominal aorta once it passes through the aortic hiatus in the diaphragm **(Figure16) (Gilroy et al.,2020).**

3-Definition of aorta

The aorta is a large artery arising from the base of the heart and extending down to the abdomen. It can be divided into five sections: ascending aorta, arch of aorta, descending aorta, thoracic aorta, and abdominal aorta. It gives rise to the main coronary arteries and the brachiocephalic trunk **(Figure17)(Zhu,2015).**

The aorta is the largest artery in the body, it receives blood pumps from the left ventricle and distributes it distally to the branch arteries. While it is one continuous vessel, its segments have been distinguished anatomically. The aorta begins in the anterior mediastinum above the aortic valve as the ascending aorta, the most proximal portion of which is also called the aortic root. This is followed in the superior mediastinum by the aortic arch, which gives rise to the brachiocephalic arteries. The descending thoracic aorta then courses in the posterior mediastinum to the level of the diaphragm, after which it becomes the abdominal aorta that then bifurcates distally into the common iliac arteries**(Isselbacher,2006).**

the aorta is the largest artery of the body, with a diameter of(2–3 cm) and divide into progressively smaller vessels**(Iaizzo,2005).**

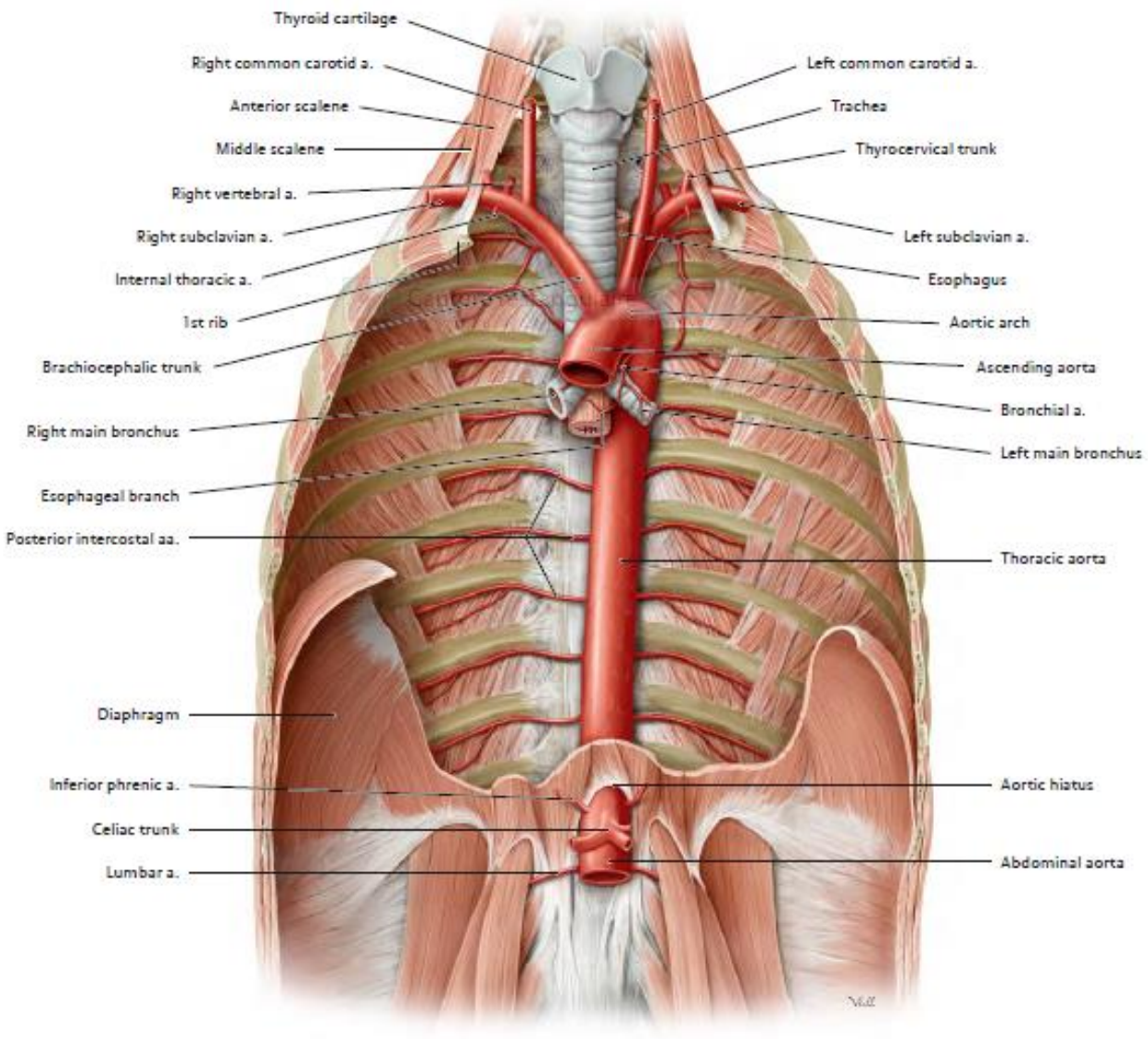


Figure 16. Thoracic aorta**(Gilroy et al.,2020).**

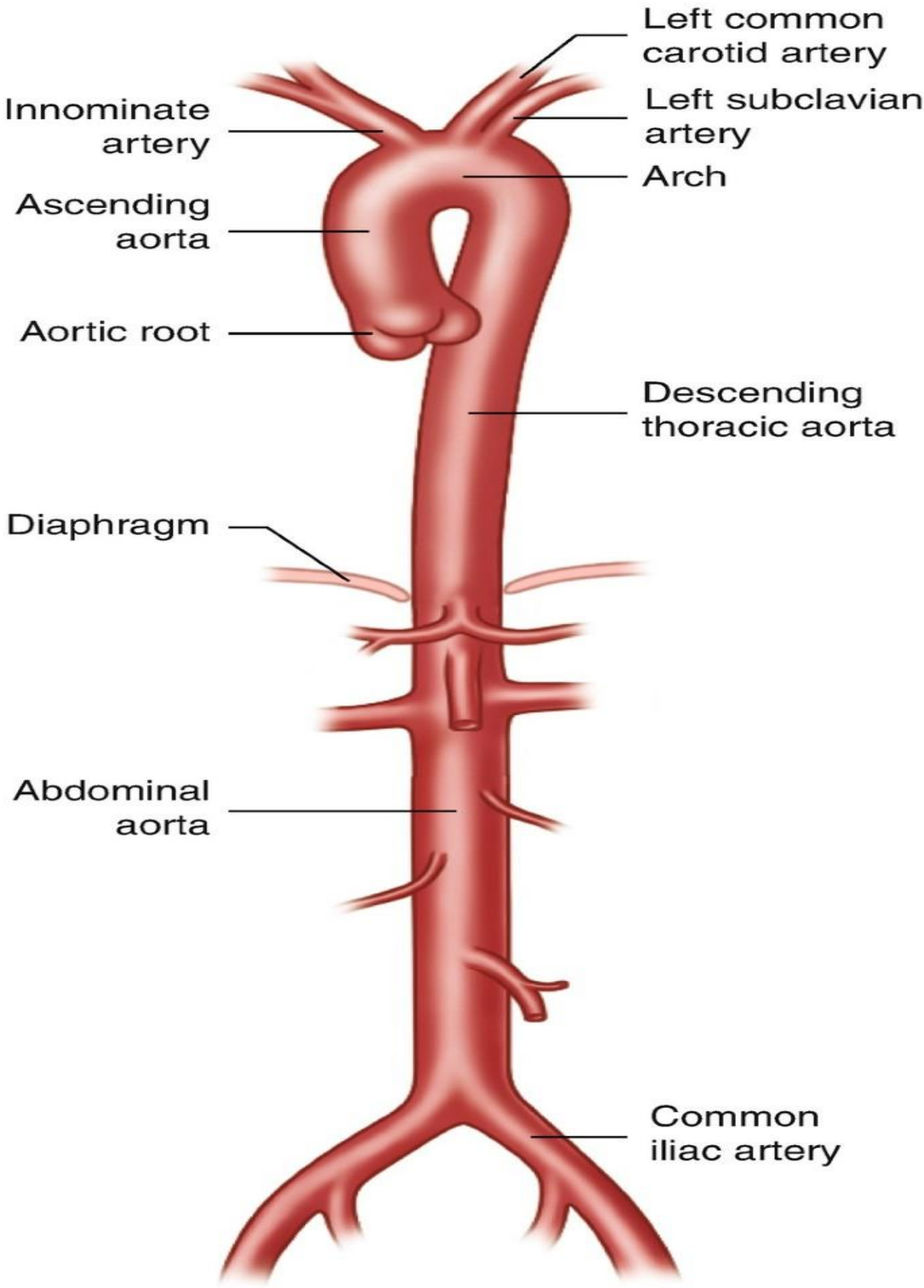


Figure 17.Thoracic aorta**(Poorsattar and Timothy,2022).**

4-**Tracheo bronchial tree**

The bronchial tree receives its nutrients via the bronchial arteries, found in the adventitia of the airways. Typically, there are one to three bronchial arteries arising directly from the aorta. Origin from a posterior intercostal artery may also occur **(Figure18) (Gilory et al., 2020).**

5-Structure and function

The aortic arch is the segment of the aorta that helps distribute blood to the head and upper extremities via the brachiocephalic trunk, the left common carotid, and the left subclavian artery **(Figure19).**

The aortic arch also plays a role in blood pressure homeostasis via baroreceptors found within the walls of the aortic arch. These receptors respond to stretching of the aortic wall and send a signal to the nucleus of the solitary tract in the brainstem via the vagus nerve, which can subsequently inhibit or disinhibit the sympathetic nervous system or activate the parasympathetic nervous system. This is one of the major mechanisms that helps prevent quick, drastic changes in blood pressure.

The aortic arch also has peripheral chemoreceptors known as aortic bodies that monitor blood composition, specifically the partial pressure of carbon monoxide and oxygen. Changes in either gas level will result in a signal being sent to the dorsal respiratory group in the brainstem via the vagus nerve, which will regulate breathing accordingly **(kelley et al., 2022).**

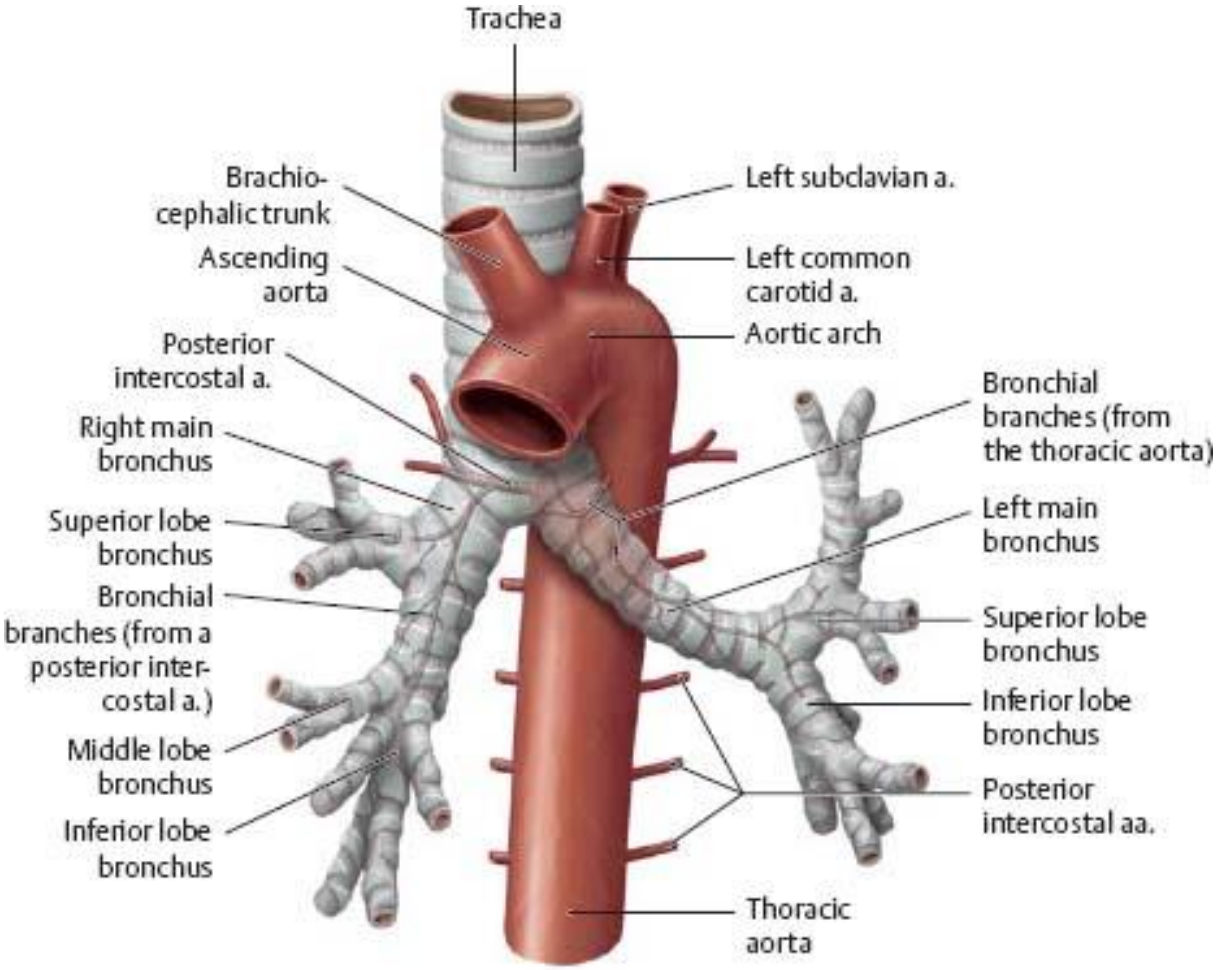


Figure 18 . Arteries of the tracheobronchial tree **(Gilory et al.,2020).**

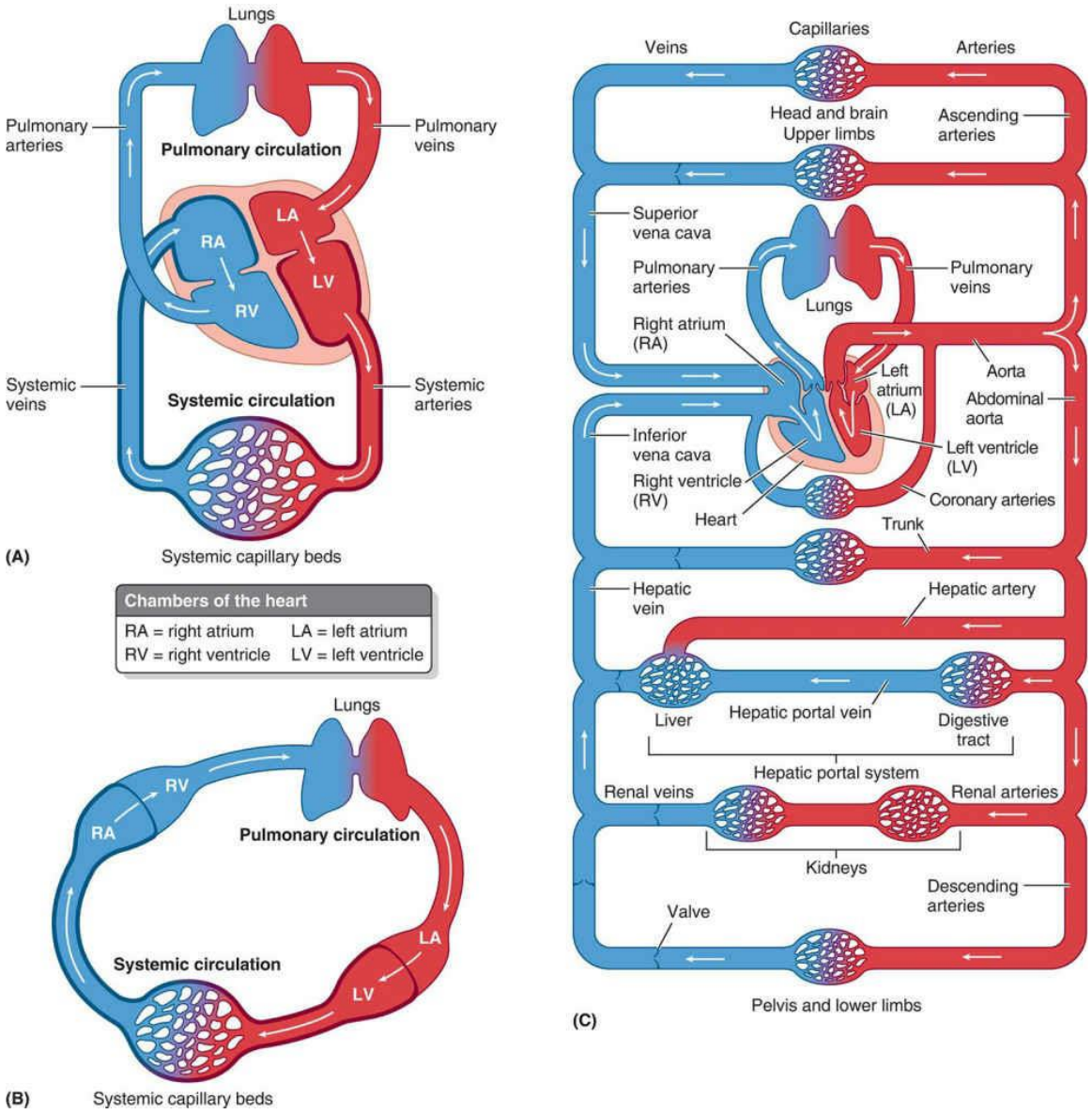


Figure 19. Circulation **(Keith et al.,2018).**

A. Schematic illustration of the anatomic arrangement of the two muscular pumps (right and left heart) serving the pulmonary and systemic circulations.

B. Schematic illustration of the body's circulation, with the right and left heart depicted as two pumps in series. The pulmonary and systemic circulations are actually serial components of one continuous loop.

C. A more detailed schematic illustration demonstrating that the systemic circulation actually consists of many parallel circuits serving the various organs and regions of the body.

6-layers and structure

The medial layer of the aorta confers elasticity and strength to the aortic wall and is composed of alternating layers of smooth muscle cells (SMCs) and elastic fibres. The SMC elastin-contractile unit is a structural unit that links the elastin fibres to the SMCs and is characterized by the following:

(1) layers of elastin fibres that are surrounded by microfibrils.

(2) microfibrils that bind to the integrin receptors in focal adhesions on the cell surface of the SMCs.

(3) SMC contractile filaments that are linked to the focal adhesions on the inner side of the membrane **(Karimi and Milewicz,2016).**

Elastic arteries, such as the ascending aorta and pulmonary trunk, receive blood flow directly from the heart ventricles in systole and are consequently the most compliant type of arteries . Elastic arteries consist of three concentric layers as follows:
The tunica intima : which is composed of the vascular endothelium and a sub endothelial layer.

The tunica media : which is the thickest layer and contains concentrically elastic fenestrated membranes and smooth muscle cells.
The tunica adventitia : which is the most abluminal layer of the elastic arteries. It is composed of elastic and collagenous fibres that are interspersed with connective tissue cells, blood vessels (the vasa vasorum) and nerve fibres (the nervivasorum).These three wall layers must to be preserved during allograft valve harvesting, processing and cryopreservation**(Figure20) (Kubiková et al.,2017).**

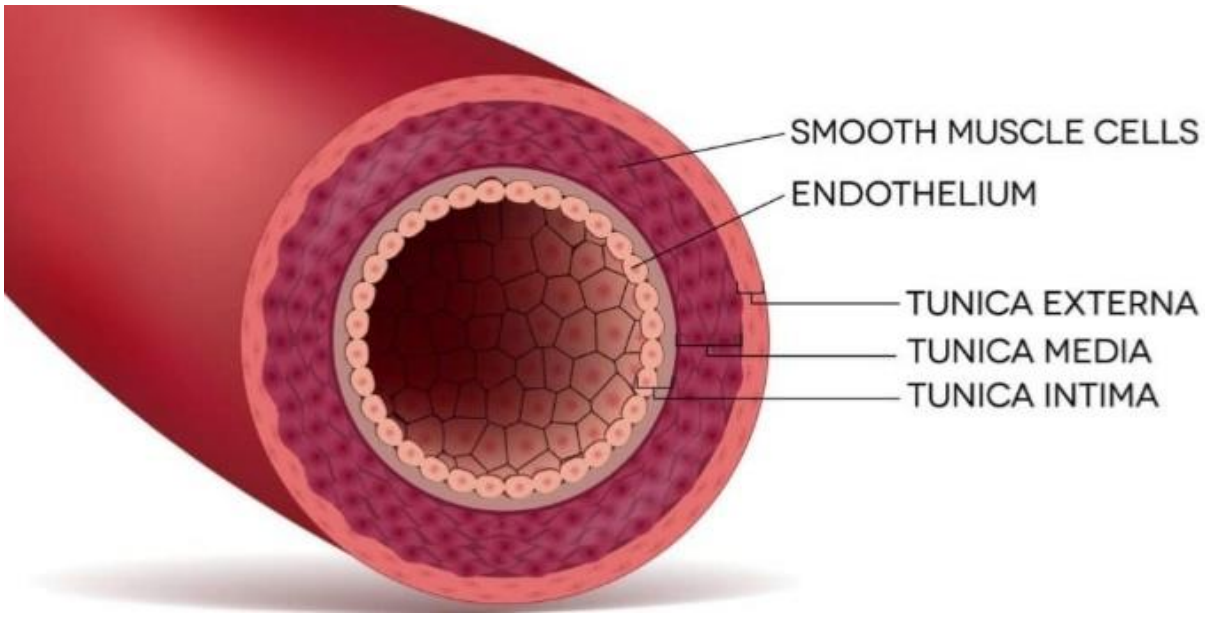


Figure 20 .layers of arterial wall (11).

7-**Aortic dissection**

Aortic dissection is a rare pathology of the aorta involving separation of the layers of the aortic wall—specifically, the tunica intima and the tunica media. The type of aortic dissection involved is classified by where the separation occurs on the aorta**(Figure21)(Samantha and Kelsy,2017)**.

There are two main anatomic classifications used to classify aortic dissection.

The stanford system is more frequently employed. It classifies dissections into two types based on whether ascending or descending part of the aorta involved

Type A involves the ascending aorta, regardless of the site of the primary intimal tear. Type A dissection is defined as a dissection proximal to the brachiocephalic artery.

- Type B aortic dissection originating distal to the left subclavian artery and involving only descending aorta.

The DeBakey classification is based upon the site of origin of the dissection.

- Type 1 originates in the ascending aorta and to at least the aortic arch.
- Type 2 originates in and is limited to the ascending aorta.

- Type 3 begins in the descending aorta and extends distally above the diaphragm (type 3a) or below the diaphragm (type 3b).

Ascending aortic dissections are almost twice as common as descending dissections **(Lévy et al.,2022).**

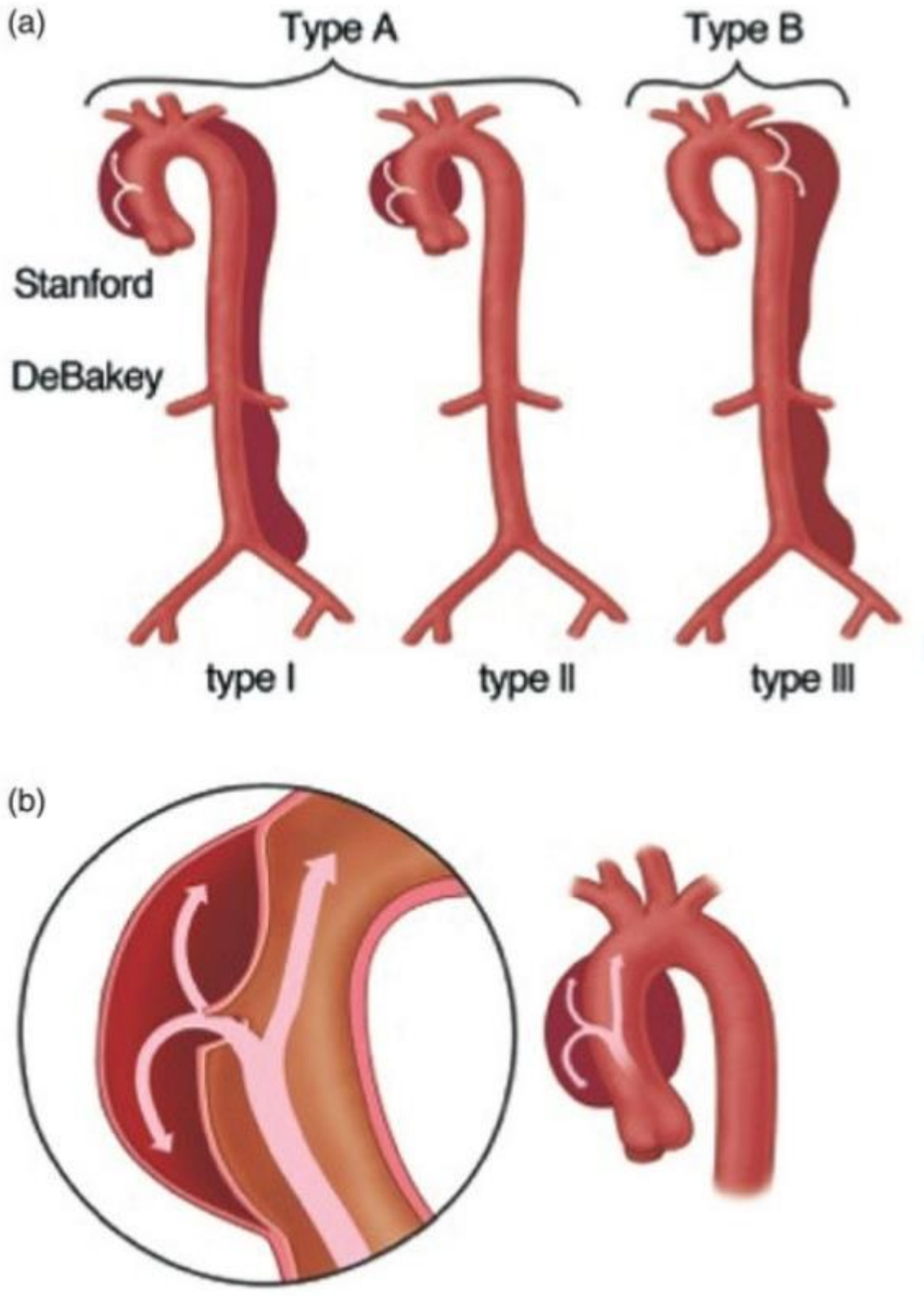


Figure21 .Types of aortic dissection (12).

(a) Types of aortic dissection according to the Stanford classification system (shown at top) and the DeBakey classification system (shown at bottom).

(b) Intimal tear and propagation of the dissection between the media and intima layers of the ascending aorta.

8-Anomalie

variations in the disposition of the 3 "classic" branches or the number of arteries arising from the arch can occur **(Gorun et al.,2010).**

Aortic arch anomalies refer to a variety of congenital abnormalities of the position or branching pattern, or both, of the aortic arch. While certain patterns of aortic arch anomalies are simple positional abnormalities, there are other patterns that form a complete or incomplete vascular ring around the trachea and esophagus causing compression of the latter structures. Aortic arch anomalies may lead to respiratory distress in the neonate or the development of milder symptoms and signs of tracheal or esophageal compression later in life, or they may remain clinically silent. Aortic arch anomalies are often associated with other congenital cardiac defects or chromosomal anomalies, such as microdeletion of chromosome 22, although they may occur in isolation **(yoo et al.,2003).**

9-Surgical consideration

The main surgical consideration of the aortic arch is avoidance of the left recurrent laryngeal nerve. The left recurrent laryngeal nerve travels posterior to the distal aortic arch, loops around, and travels back up and anterior to the aortic arch. Damage to this nerve during surgery can result in voice hoarseness or vocal cord paralysis **(kelley et al.,2022).**

Chapter VI

Hot water

VI- Hot water

1-Definition

Water is an essential compound for the existence of life as we know it **(Mottl et al., 2007)**.It is the most important constituent of all living organisms (70% of the total mass and 99% of all molecules) **(Giudice et al., 2009)**.It is of fundamental importance for human life and plays an important role in many biological and chemical systems **(Ludwig, 2001)**.

Water is the principal chemical constituent of the human body. total body water represents 50% to 70% of body weight. Variability in total body water is primarily due to differences in body composition. Lean body mass is about 73% water and fat body mass is 10% water. Total body water is distributed into intracellular fluid and extracellular fluid compartments, which contain about 65% and 35% of total body water, respectively **(Sawkaet et al., 2005)**.

It is the medium in which all life occurs. Biological molecules are bathed in it, and the interactions of proteins, nucleic acids and membranes with water shape their structures and functions **(Rascke, 2006)**.

2-Structure

Water molecules are V-shaped with molecular formula H2O **(Xiao, 2014)**. two hydrogen atoms bonded to one oxygen atom **(Shakhashiri, 2011)**. which is symmetric (point group C2) with two mirror planes of symmetry and a two-fold rotation axis. The hydrogen atoms may possess parallel or antiparallel nuclear spin **(Figure 22)(Xiao, 2014)**.

The structure is affected by the temperature and the external pressure. A rise in the temperature of a liquid causes its expansion and a decrease of its density, whereas rising pressures above ambient cause an increase in the density **(Figure 23)(Marcus, 2009)**.

Other basic properties of water are its size, shape and polarity. Water is a very polar molecule with the ability to make strong electrostatic interactions with itself, other molecules and ions **(Sharp,2001)**.

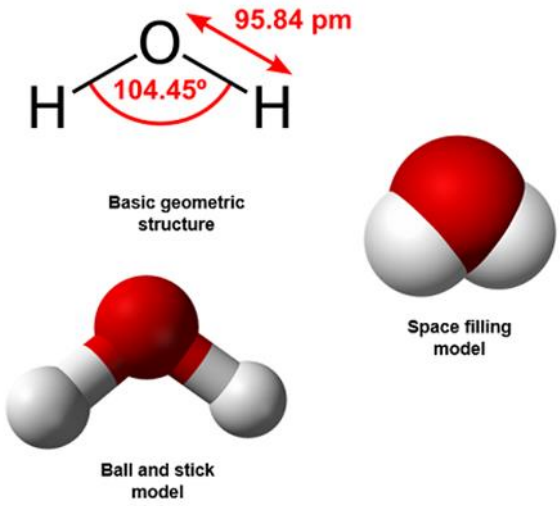


Figure 22. Water molecules (13).

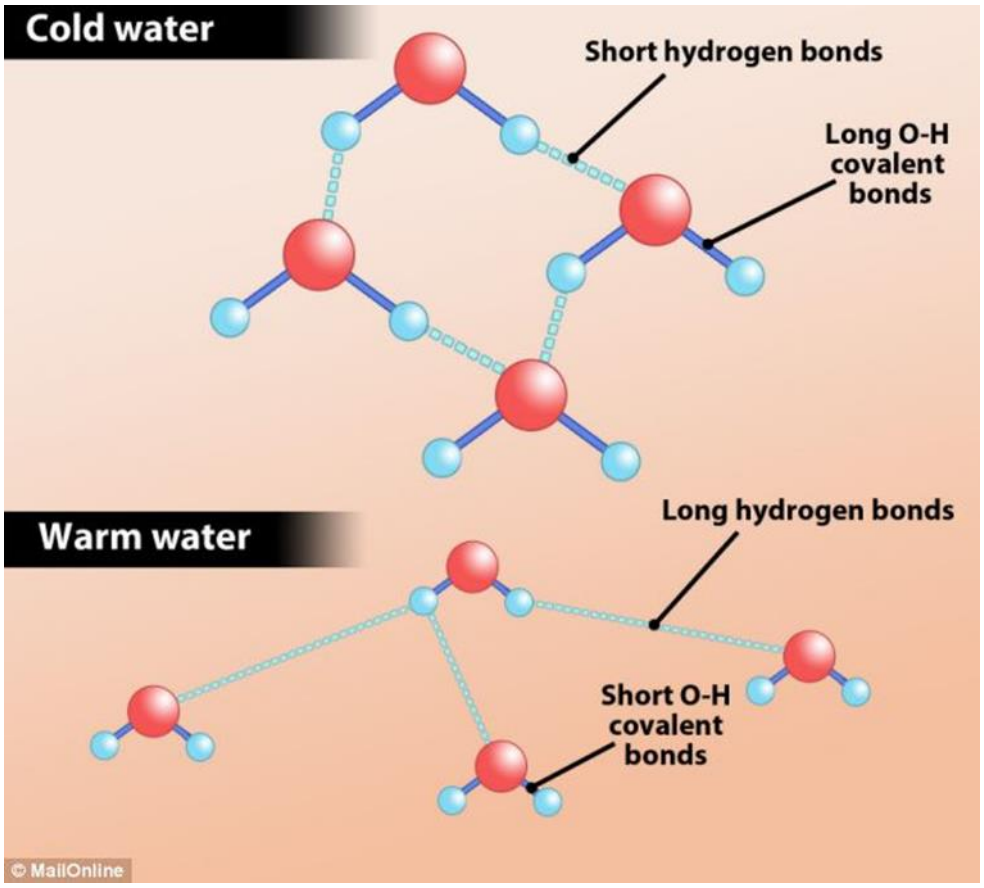


Figure 23. Cold and warm water structure (14).

3-Hydrotherapy

3.1-Definition

During the 1800s, Sebastian Kneipp, the 'founder of hydrotherapy', wrote extensively about the healing effects of water. His research was immediately recognized by healthcare professionals **(Hall et al., 2008)**.

Hydrotherapy is derived from the Greek word "Hydro" meaning water, and "Therapia" meaning healing. It means water healing. It is controlled aquatic exercise in heated sanitized water. Any treatment in water **(Bahadorfar, 2014)**.

Hydrotherapy is the external or internal use of water in any of its forms (water, ice, steam) for health promotion or treatment of various diseases with various temperatures, pressure, duration, and site **(Mooventhan and Nivethitha, 2014)**.

Three types of hydrotherapy can be used: neutron therapy, thermo-therapy and cryo-therapy the difference being the varying temperature of the water **(Devkate et al., 2016)**.

These health benefits come from the mechanical and thermal effects of water interacting with the body. It includes the use of physical water properties, specifically temperature and pressure, and sometimes the delivery of minerals or herbal treatments to manipulate the body's flow of blood, the endocrine system and associated neural systems in order to treat the symptoms of certain diseases **(Bahadorfar, 2014)**.

Tabel 3. Techniques and uses of hydrotherapy **(Chowdhury et al., 2021)**.

Techniques of hydrotherapy	hydro-massage, colon hydrotherapy, baths and showers, cold foot bath, heating compress, hip or sitz bath, steam bath, steam inhalation, and full immersion bath.
Uses of hydrotherapy	For pain relief, for circulationm for immunity, stress, complexion, arthritis, back, pain, hydrotherapy for acne, insomnia, joint pain, headaches, colonic hydrotherapy for stomach problems, sciatica, hydrotherapy for sleep disorders, labor, temperature regulation.

4-Benefits of drinking hot water

Drinking hot water leads to healthier digestion and consuming it daily leads to help in body 0detoxification and helps in improving blood circulation , prevents from ageing and clears skin and prevents premature ageing like wrinkles **(Subaraman et al., 2020)**.

It can relieve pain for patients with various conditions **(Bender et al., 2005)**.It can also improve their sensory perception by blocking the nociception signals **(Yamazaki et al., 2000)**. Additionally, it can help nourish the body and reduce the effects of lactic acid and other chemicals in the body **(Fam, 1991)**.

Prevent various diseases, symptoms and allergies and improve brain memory **(Alhadjri, 2010)**.Consumption of hot beverages stimulates the overall physiological process faster than normal rate. It will be beneficial to patients who have arthritis **(Subaraman et al., 2020)**.

Chapter VII

Traditional yeast

VII-Traditional yeast

1-Definition

Yeasts are unicellular fungi with a typical vegetative growth by budding or fission **(De et al., 2016)**.

Wild yeasts consume the carbohydrates in the flour and produces alcohol and carbon dioxide gas as the primary by products (bubbles) **(Bunning et al., 2022)**.

sourdough yeasts fermented the flour sacharides (maltose, sucrose, glucose, and fructose) via the Embden-Meyerhof-Parnas (EMP) pathway into pyruvate, thereby generating both ATP and reducing power (NADH + H+), and further convert pyruvate into ethanol and carbon dioxide (alcoholic fermentation), thereby regenerating the cofactor NAD+ consumed in the upper part of the EMP pathway **(Figure 24)(De et al., 2021)**.

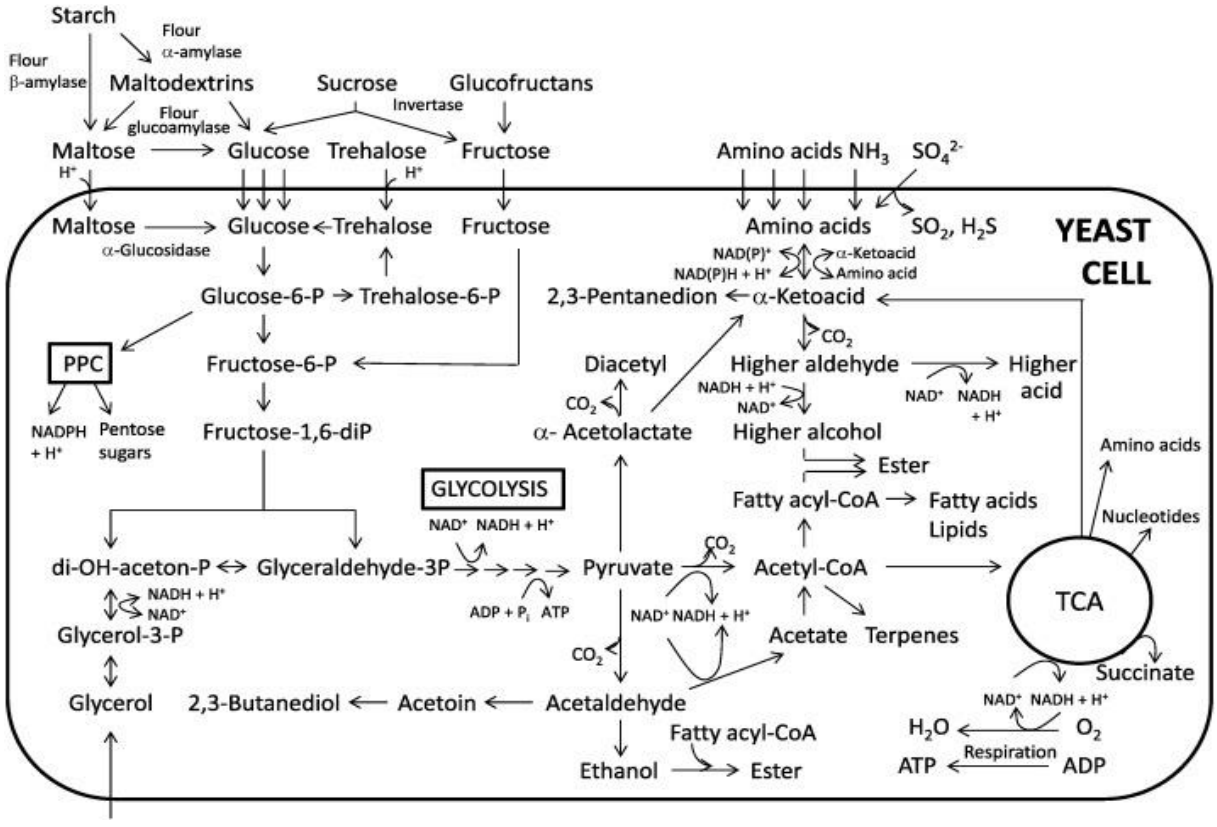


Figure 24. Overview of the metabolism of yeasts in a sourdough matrix **(De et al., 2021)**.

Yeasts are responsible for the aroma and flavor of many fermented foods and beverages such as bread, soy sauce, cheeses, beer, wine, and sake **(Punyauppa al., 2022)**.

Yeasts species the most widespread yeast species in sourdough are "*Saccharomyces cerevisiae*",

"*Kazachstania humilis*" (previously named *Candida humilis*), "*Kazachstania exigua*",

"*Pichiakudria vzevii*", and "*Torulaspora delbrueckii*" **(Carbonetto et al., 2020)**.

2-Sourdough starter

Sourdough starter, which is also known as natural yeasts, it's the oldest form of leavening bread. The utilization of different types of flour during fermentation of sourdough also leads to the diversity of wild yeasts species **(lau et al., 2021)**.

3-Types of sourdough starter

The term wild yeasts refer to strain coming from the direct environment, three types of sourdough starter can be distinguished which influence the microbiology of the mature sourdough **(Figure 25)(De et al., 2021)**.

The utilization of different types of flour during fermentation of sourdough also leads to the diversity of wild yeasts species **(Lau et al., 2021)**.

Type I sourdough starters are most commonly used in artisanal bakeries and are usually kept at ambient temperature (20–30 °C), though they can be refrigerated when not in use or at regular intervals **(Calvert et al., 2021)**.

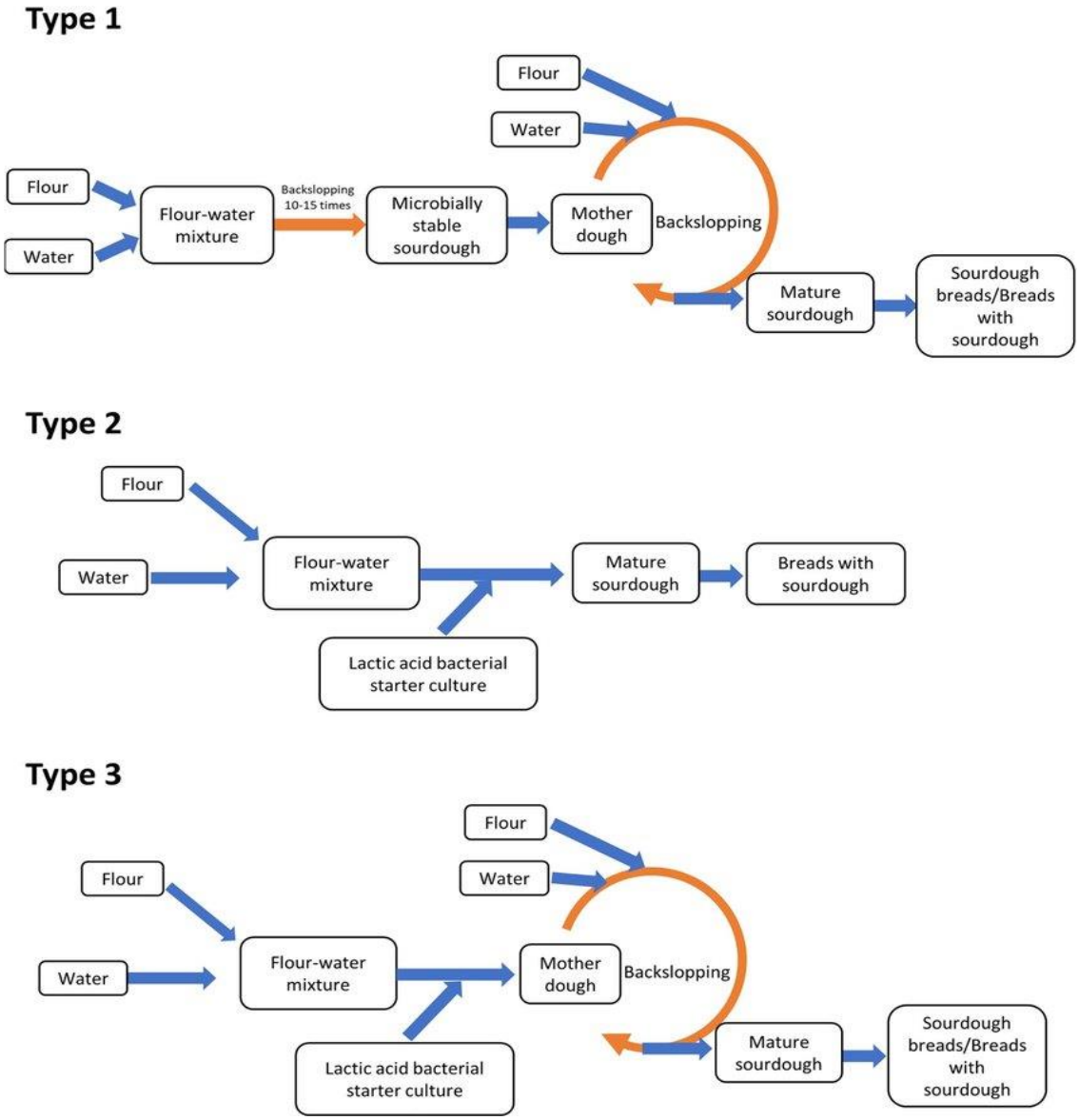


Figure 25. Types of sourdough starter (15).

4-Formulation yeasts

Sourdough starter can be considered as a mixture of water and flour fermented by yeasts and bacteria **(Albagli et al., 2023)**.

Wild yeasts consume the carbohydrates in the flour and produces alcohol and carbon dioxide gas as the primary by products (bubbles) **(Bunning et al., 2022)**.

In sourdough fermentation, yeast and lactic acid bacteria work together to form the natural flora **(Kezer et al., 2022)**.

sourdough yeasts fermented the flour sacharides (maltose, sucrose, glucose, and fructose) via the Embden-Meyerhof-Parnas (EMP) pathway into pyruvate, thereby generating both ATP and reducing power (NADH + H+), and further convert pyruvate into ethanol and carbon dioxide (alcoholic fermentation), thereby regenerating the cofactor NAD+ consumed in the upper part of the EMP pathway **(Figure 26)(De et al., 2021)**.

5-Benefits of traditional yeast

Excellent source of vitamins, minerals, and high-quality protein, it support the immune system and reduce inflammation resulting from bacterial infection. It may also be helpful in treating diarrhea **(Marengo, 2023)**.

-Good for Your Gut

The fermentation process for sourdough bread can lead to an increased number of prebiotic- and probiotic-like properties, which help improve gut health **(Ball, 2018)**.

-Can Lead to Better Digestion

Even though sourdough bread is not gluten-free, a 2021 review in the journal Foods found that sourdough consumption might help improve the digestion of gluten. The fermentation process for sourdough alters the enzymes in the wheat and might potentially help counteract adverse reactions to gluten **(Ball, 2018)**.

-It may promote weight loss

The high prebiotic profile in sourdough improves digestion and absorption of nutrients, which promotes glucose regulation and metabolism, causing one to burn fat and loses weight **(Marengo, 2022)**.

Good for nerve function: Dry yeast has thiamine, riboflavin, vitamin B6 and folate, which promotes healthy aging (Katherin, 2018).

Whole grains and bread, like sourdough bread, are a staple of the Mediterranean diet. Some research has pointed out it could also be a crucial food to help promote healthy aging. Fermented grain-based products, like sourdough, have antioxidant, anti-hypertensive, anti-diabetic **(Ball, 2018)**.

Provides vital nutrients during pregnancy: Dry yeast is an excellent source of folate. Folate can help reduce the risk of birth defects and optimize foetal growth and development **(Marengo, 2023)**.

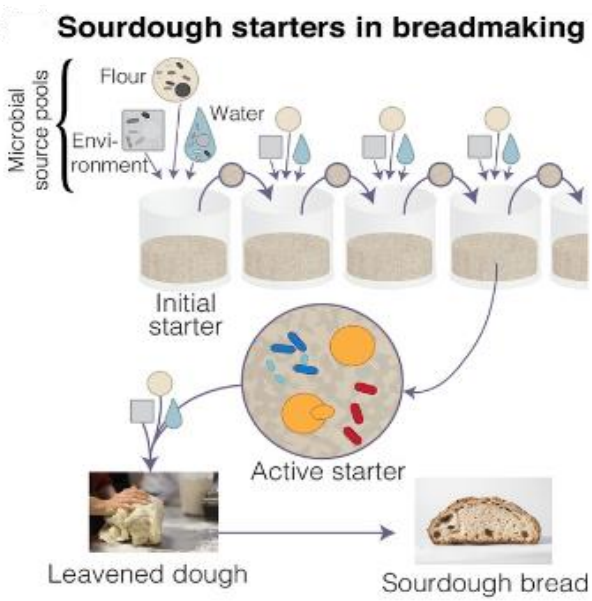


Figure26 . Sourdough starters in breadmaking (16).

Experimental Study

Chapter VIII Material and methods

Material and methods

I. Material

I.1. **Chemical products**

Chemical products used in our study are:

Chloroform, NaCl 0.9%, formalin 10%, dithiobis-2-nitrobenzoic acid (DTNB), sulfo-salicylic acid (0.01M), Bovine Serum Albumin (BSA), orthophosphoric acid (85%), Tris Ethylene Di-amine Tetra Acetic acid (EDTA, 0.02M), tris buffered phosphate buffered saline (PBS), tris buffered saline (TBS), different concentrations of ethanol (25%, 60%, 70%, 95% and 96%), HCl, NaOH, NaCl, butanol, xylene, paraffin and glycerin, acetic acid, heamatoxylin eosin, NaH2PO4, Na2HPO4, Coomassie Brilliant Blue G-250.

I.2. **Equipments**

Precision weighing balances (readability 0.01g) to determine the weight of the mice, precision Weighing Balances (readability 0.0001g) to determine the quantity of sugar and yeast, , heating magnetic stirrer, pH meter, centrifuge, spectrophotometer, oven, microtome, vortex mixer, eppendorf tubes, paraffin molds, tissue cassettes, lithium heparin tubes, small bottles.

Photo1 . Materials used during experimental work.

I.3. **Choice of treatment**

In this research we have used hot water at 50°C proposed by ALHAJRI (2010) and ALHAJRI – (2020) .The concentration of Crystallize sugar of (200mg/kg) and yeast (50g/65kg)were used in this study.

I.4. **Animals**

In this study we have used 36 mice Albino *Mus musculus* obtained from the animal house at University frères Mentouri-Constantine1 (Algeria).

II-Methods

II.1 Treatment of mice

The study was carried out on a group of 36 adult male Albino *Mus Musculus* mice, aged between 2 to 3 months and weighing between 28-41g.After obtaining the animals, they were separated and housed in plastic cages covered with wire mesh coated with anti-rust paint, with a layer of sawdust placed at the bottom of each cage, and replenished daily. They were placed under standard laboratory conditions of temperature, humidity, and light and free access to water and diet . Animals were acclimated to laboratory conditions for a week prior to the experiment.

Animals were divided into six groups of similar mean body weights and fed for 21 days with control and experimental diet as shown down :

Group control (C,G1): was fed with standard diet and drunk water at room temperature.

Group sugar (S, G2): was fed with standard diet rich in sugar and drunk water at room temperature .

Group hot water (Hw, G3): was fed withstandard diet and drunk hot water at fifty degrees.

Group yeast (Y, G4): was fed with standard diet rich with traditional yeast and drunk water at room temperature.

Group sugar + hot water (SHW, G5): was fed with standard diet rich with traditional yeast and drunk hot water at fifty degrees.

Group sugar + yeast (SY, G6): group was fed with standard diet rich in sugar with traditional yeast and drinking water at room temperature (Table 4). The diet and weight were measured every day at the same time during 21days of treatment.

II.2 Blood and tissue sampling

After 21 days of treatment, blood samples were collected after fasting the animals from retro orbital plexus into heparin tubes by using glass capillaries and the blood was taken directly to the analysis laboratory (EL AMINE laboratory Constantine Algeria).

After the blood samples collection, the animals were sacrificed. Then, the aorta removed and rinsed with saline solution (0.9%), and fixed in formalin 10%, and the liver are stored in the freezer without rinsing them with a saline solution at-20°c for the dosage of the antioxidant (GSH).

Table4. Treatment of mice for 21 day.

Experimental group	Treatment	Number of animals	Duration of experiment	Daily dose
G 1 (C)	Normal water Standard diet	6	21	125ml / day 120 g / day
G 2 (S)	Normal water Standard diet+ Sugar	6	21	125ml / day 120 g / day 200g/65kg/ day
G 3 (HW)	Hot water Standard diet	6	21	125ml / day 120 g / day
G 4 (TY)	Normal water Standard diet + Yeast	6	21	125ml / day 120 g / day 50g/65kg/ day
G 5 (S+Hw)	Hot water	6	21	125ml / day

	Standard diet Sugar			120 g / day 200g/65kg/ day
G 6 (TY+S)	Normal water Standard diet+ Sugar Yeast	6	21	125ml / day 120 g / day 200g/65kg/ day 50g/65kg/ day

III . Biochemical investigations

A- The blood analysis

The blood analysis was carried on some parameters such as blood sugar, creatinine, T-ch, TG, HDL-C, LDL-C, CRP, ASATand ALAT.

B- Determination of antioxidant

1- Tissue homogenate preparation

0,5g of the liver was homogenized in 2ml of TBS (Tris 50 mM, NaCl 150 mM, pH 7.4). The homogenates were centrifuged at 9000 g for15 min at 4˚C. The supernatant was keeped in the freezer at -20C until the determination of proteins and reduced glutathione concentrations.

2- Glutathione reduced measurement

Liver homogenate sample (0.8ml) was deproteinized with (0.2ml) of 5-sulfosalicylic acid solution (0.25%) and was allowed stand on ice for 10 min. Following centrifugation at 1000 tours/mn) during 5minutes to remove the precipitated protein. (0.5ml) of supernatant was mixed with 1 ml Tris/EDTA buffer (pH 9.6) and (0.025 ml) of DTNB-reagent (0.01M 5,5'dithiobis-2-nitrobenzoic acid) and left at room temperature for 5 min. Then the absorption was measured at 412 nm using a spectrophotometer (SHIMADZU UV-1280) against the blank reaction **(photo2).**

3 - Protein determination

We have measured the protein concentration by the method of Bradford (1976), using bovine serum albumin as a standard. Where the absorbance is proportional to the protein present in the solution.

A 0.1 mL liver homogenate sample was mixed with 5 mL of Bradford's reagent and left for 5 min. Then the absorbance was measured at 595 nm using a spectrophotometer in comparison with blank reaction.

The protein concentration in the test samples is determined from the calibration graph (**Figure39).**

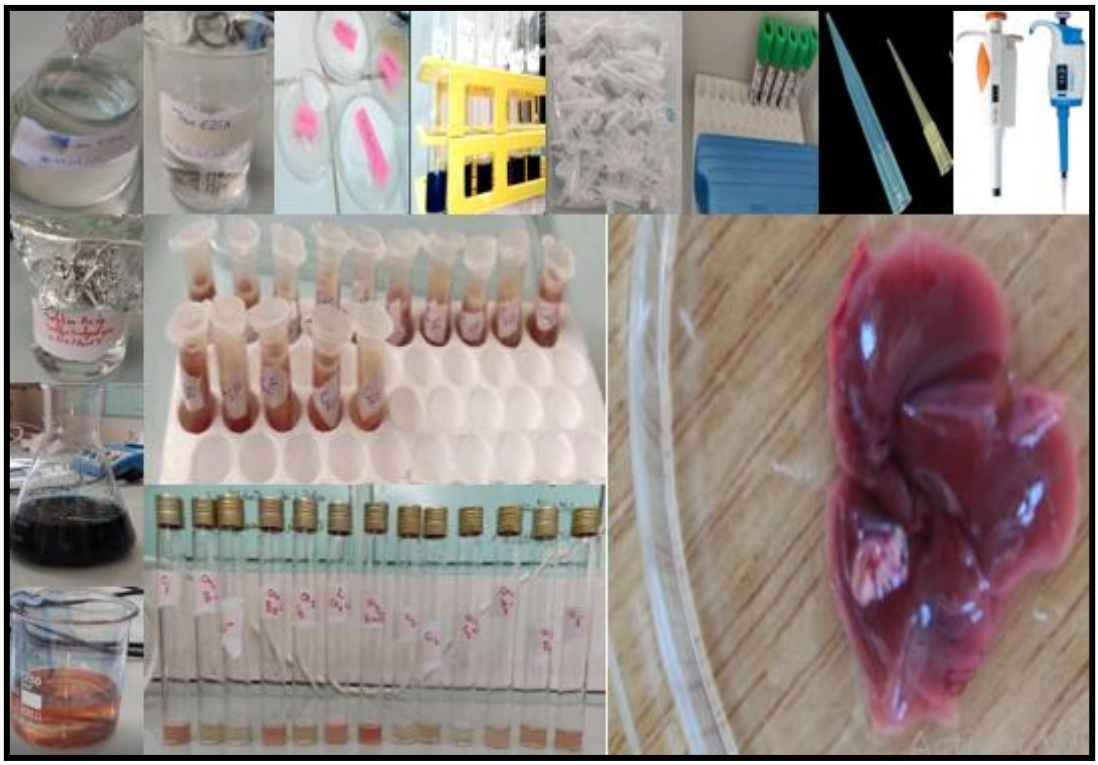


Photo2. Materials and solutions used in protein and glutathione determination.

IV . Preparation of histological sections

1. Fixation

The aorta was taken from the formol solution and placed in the alcoholic bouin solution for 5 min.

2. Dehydration

Dehydration was performed through a series of ethanol solution baths:

- First bath: 60% ethanol (3 x 20 minutes)
- Second bath: 75% ethanol (3 x 20 minutes)
- Third bath: 96% ethanol (3 x 20 minutes)

Samples were kept in small bottles with butanol for 3 days. Then they were cleared in xylene for 10 min with two exchanges.

3- Insertion into paraffin

In this step, the aorta was immersed in paraffin at 60°C for 2 hours. In two exchanges, samples were placed into paraffin molds and then into tissue cassettes. Then the cut was made with a thickness of 5 μm using a microtome.

4- Coloring stage

The samples were placed in two xylene baths for 10 minutes each.After this time they were placed in ethanol baths with decreasing concentrations:

- First bath: 96% ethanol 5 min
- Second bath: 75% ethanol 5 min
- Third bath: 60% ethanol for 5 minutes

The samples were placed in heamatoxylin for 4 minutes, and then washed with tap water. After that the sample coloured with eosin for 5minutes,after this time they were washed with tape water.

The samples immersed in ethanolfor 1 minute, then placed in two xylene baths for 2 minutes each.

Samples dried on the heating plate at 37°C. After this stage, the samples are ready for viewing under a microscope.

V. Statistical Analysis

The values obtained were expressed as mean ± SEM and subjected to statistical analysis using one-wayanalysis of variance (ANOVA), followed by Tukey's post-hoc test (PRISM 5). $P< 0.05$ values were considered as significant different.

Results and discussions

I. Results

I.1-Weight

Our results demonstrated that the weight is increased during the first week(33.06g±1.61) and the third week (36.80g±0.99) respectively in the group control ,in the group of mice treated with hot water in the first week was (33.01g±0.71) and in the third week was (33.17g±0.74)and in the group administrated with crystallize sugar in the first and the third week was (35.81g±0.41) (36.07g±1.44) respectively , in the group administered with crystallized sugar and treated with hot water (33.60g±0.99)(34.11g±3.01) on the other hand ,the weight is also increased in the groups administered with yeast in the first and third week (30.50g±1.74)(33.13g±2.32) , and in the group administered with crystallized sugar and treated with traditional yeast (29.27g±2.15)(31.60g±1.98) **(Figure27)**

I.2-Food

Our results demonstrated that the food consumed by mice is increased during the first and third week (60.14g±33.57) (83.14g±19.74) respectively in the group control, in the group of mice treated with hot water in the first week was (63.57g±18.97) and in the third week was (82.71g±29.09) and in the group administered with crystallize sugar in the first and third week (42.57±28.05) (99.57g±18.54) respectively. On the other hand, the food consumed by mice is increased in group administered with crystallized sugar and treated with hot water (80.14g±18.30) (92.42.83g±28.98) and in the group administered with yeast in the first and third week (84.14±19.11) (76.41±42.05) , however the food consumed is decreased in group administered with crystallized sugar and treated with traditional yeast (68.71±29.43) (42.83±41.03) between the first and third week (**Figure 28).**

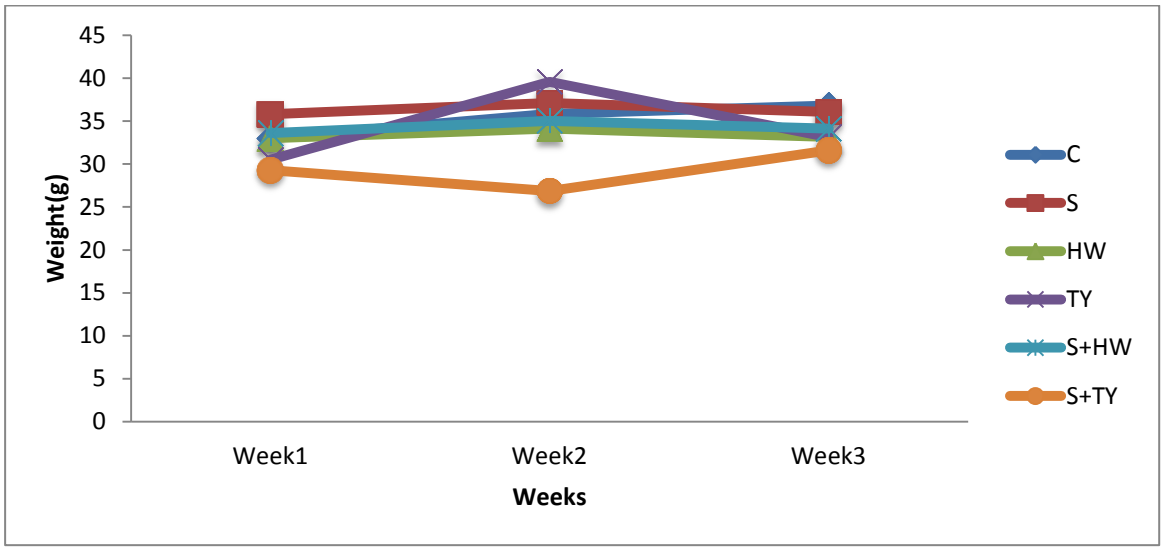


Figure27. Effect of crystallize sugar , hot water and traditional yeast on the weight of mice during 21 days**.**

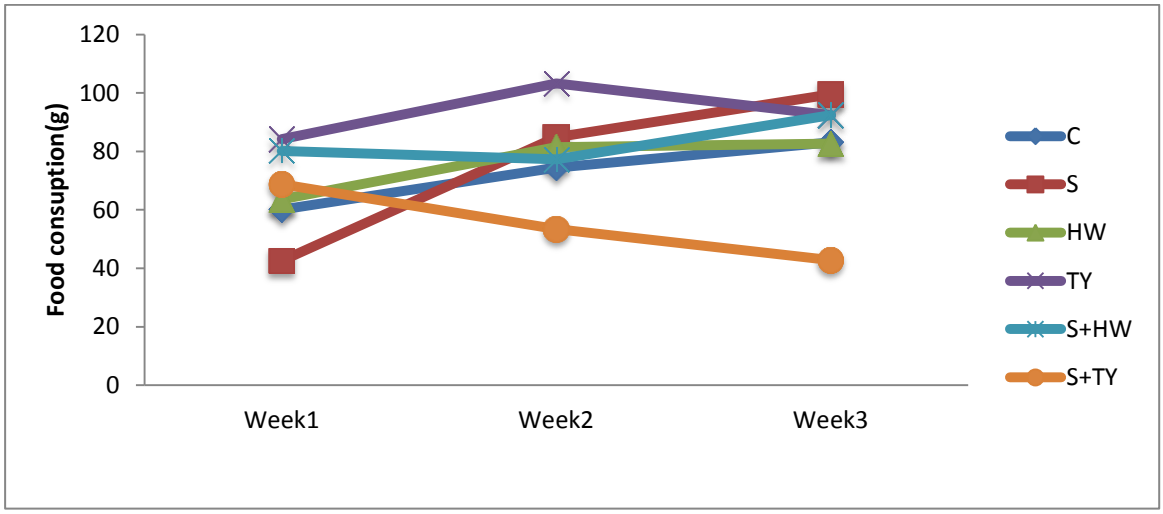


Figure28. Effect of crystallize sugar, hot water and traditional yeast on the food consumed by mice .

I.3-Blood sugar

The **(Figure29)** showed that there is a difference between groups very highly significantly C(0.45 g/L±0 .13) ,H(0.94g /l±0.2) ,S(1.15g /l±0.38),SH(0.54g/l±0.19),TY(1.81g/l±0.10),S+L(1. 66g/l±0 .37) P<0.0001 .

The Tukey test demonstrated that the level of blood sugar is increased very highly significantly in groups (S) and (TY+S) P <0.0001 and P <0.001 respectively and highly significantly in group TY P<0.01. On the other hand we obtained that the level of blood sugar in groups of animals treated with hot water is increased significantly and groups (SHW) increased but not significantly P<0.05and P> 0.05 respectively when compared to the control group .

the concentration of sugar in group of animal treated with hot water is increased but not significantly when it is compared to the group of (S).

I.4-Lipids status

I.4.1-Total cholesterol

The data showed that there is a difference between the concentration of T-ch but not significantly P> 0.05.

The tukey test showed that the concentration of total-cholesterol is increased but not significantly in the groups administered with crystallized sugar (1.44g/l±0.20) and SHW (1.68g/l±0.20) and the group administered with traditional yeast (1.50g/l±0.18) when it is compared to the group C (1,40g/l ±0.24) P> 0.05.

The total cholesterol is decreased but not significantly in groups treated with Hot water(1.23g/l±0.38) and traditional yeast when compared to the control group P>0.05 **(Figure 30).**

I.4.2-Triglyceride

The data showed a difference very highly significantly in the values of triglycerides in groups administered with crystallized sugar (S) (0.62g/l±0.13) and administered with crystallized sugar and treated with hot water (S+H) (0.68g/l±0.13) ,(S+TY) (0.55g/l±0.23) ,group (H) treated with hot water (0.84g/l±0.34) , control group (0.68g/l±0.12) and the group administered with traditional yeast (1.25g/l±0.16) P≤0.001 **.**

The tukey test showed that the concentration of TG in group (TY) is increased higly significantly when compared to groups (C and S) P≤0,01**(Figure31).**

I.4.3-HDL-C

The data showed a difference in the values of HDL-C in groups (S) were (1.15g/l±0.16) and (SHW) (1.40g/l±0.18) and (S+TY) (0.87g/l±0.28) (HW) (1.05g/l±0.31) and control (1.26g/l±0.24) and (TY) (1.30g/l±0.14) **(Figure32)** but not significantly P>0.05.

I.4.4-LDL-C

The data showed a difference in the values of LDL-C in groups (C) were (0.06g/l±0.03) and (TY) (0.08g/l±0.06) and (S) (0.18g/l±0.14) and (HW)(0.15g/l±0.07) and (SHW)(0.16g/l±0.04) and (S+TY) (0.11g/l±0.09) **(Figure 33)** but not significantly P>0.05.

I.5-CRP

The Figure34 showed that there is a difference very highly significantly in the values of CRP between groups P<0.0001. The values were (S) (0.09mg/l±0.06), (HW) (0.12mg/l±0.05), (SHW) (0.41mg/l±0.34), (yeast) (0.08mg/l±0.06), STY (0.12mg/l±0.08) when compared to the (C) (0.74mg/l±0.21) **(Figure 34).**

The turkey test demonstrated that the values of CRP in (S) (HW) (TY) are decreased very highly significantly P<0.001 and it is decreased in group (SHW) and (STY) significantly and highly significantly when compared to the control group P<0.05 and P<0.01 respectively .

I.6-Creatinine

Our data obtained showed that the concentration of creatinine is differ in all groups but not significantly P>0.05.

The turkey test demonstrated that the level of creatinine in group(S) (2.97mg/l±1.06) increase but not significantly when it is compared to the control group (2.17mg/l±1.47).

We obtained that the concentration of the creatinine is decreased in group treated with hot water (H)(1.74mg/l±0.59) and group treated traditional yeast(TY) (1.60mg/l±0.54) but not significantly P>0.05**(Figure35).**

I.7-Glutathione reduced

The concentration of glutathione reduced is decreased in groups (HW) (0.016nmol /mg protein), (TY) (0.01nmol /mg protein), (HW+S) (0.013nmol /mg protein) and (S+TY)(0.005nmol /mg protein) when compared to the (C) and (S) (0.17nmol /mg protein) (0.16 nmol /mg protein) respectively **(Figure36).**

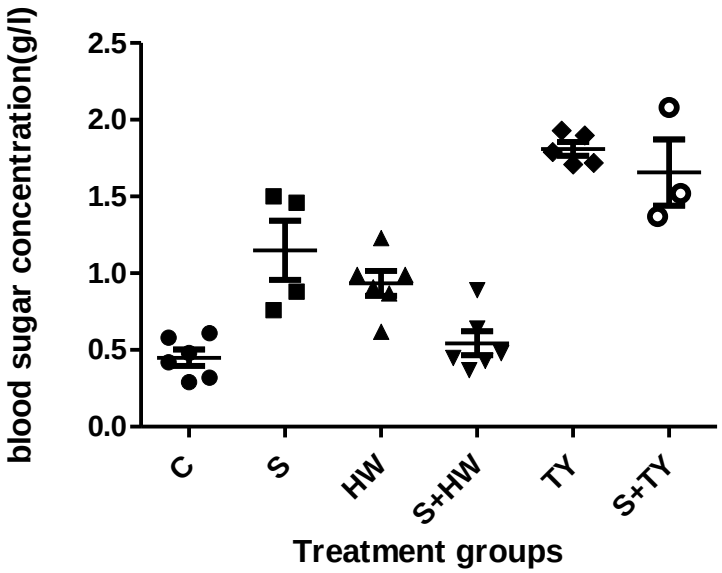


Figure 29. Effect of high consumption of crystallize sugar, hot water and traditional yeast on fasting blood sugar in mice.

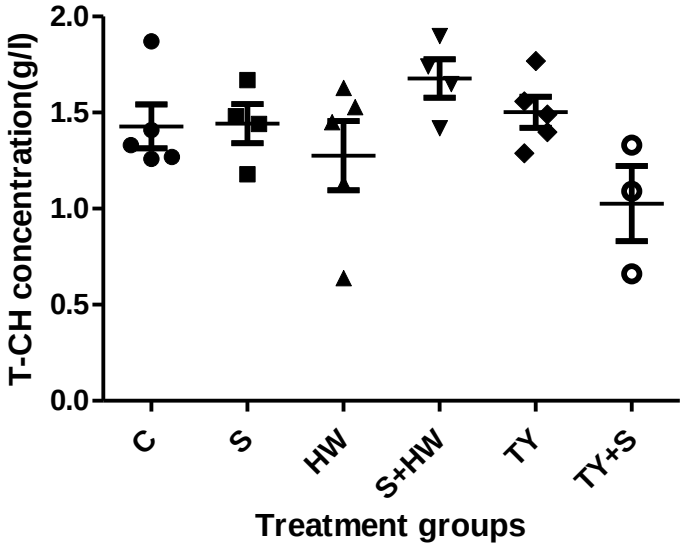


Figure 30. Effect of high consumption of crystallize sugar, hot water and traditional yeast on T-cholesterol in mice.

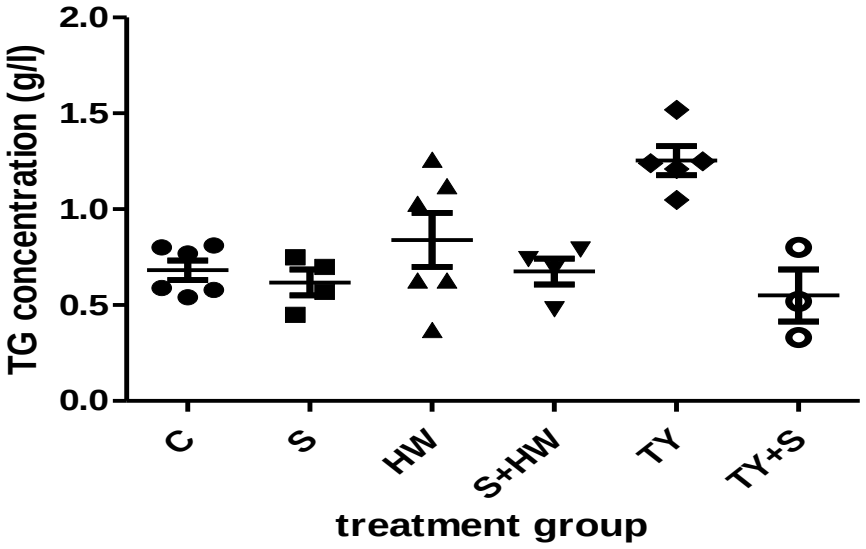


Figure 31. Effect of high consumption of crystallize sugar, hot water and traditional yeast on triglyceride in mice.

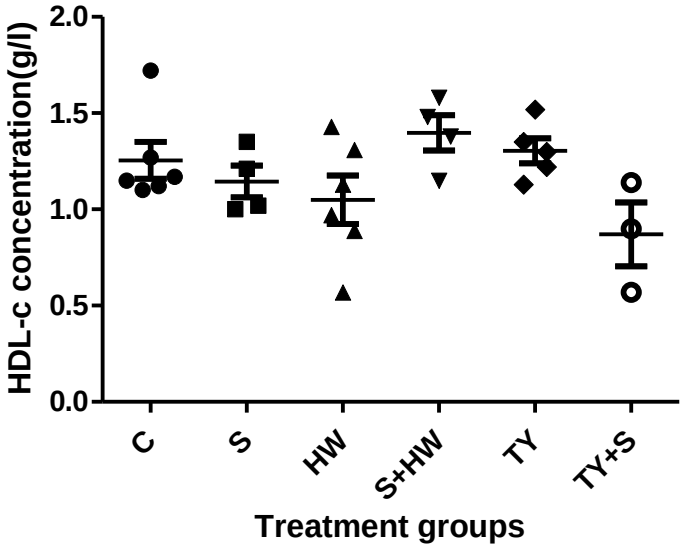


Figure 32. Effects of high consumption of crystallize sugar, hot water and traditional yeast on HDL-C in mice.

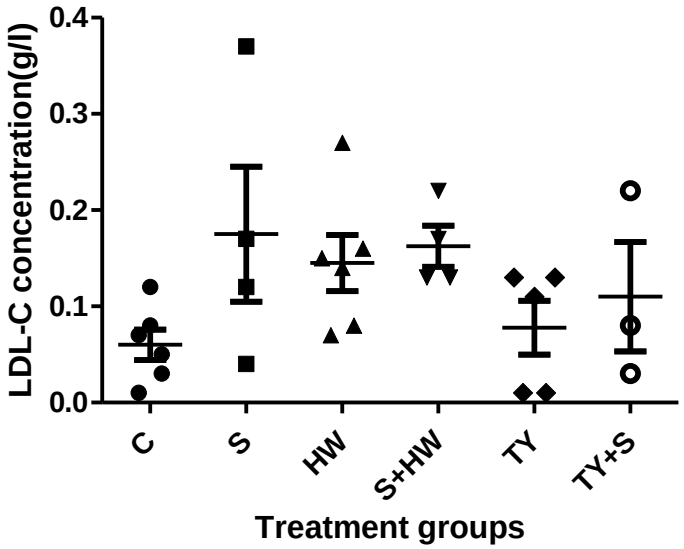


Figure 33. Effect of high consumption of crystallize sugar, hot water and traditional yeast on LDL-c in mice.

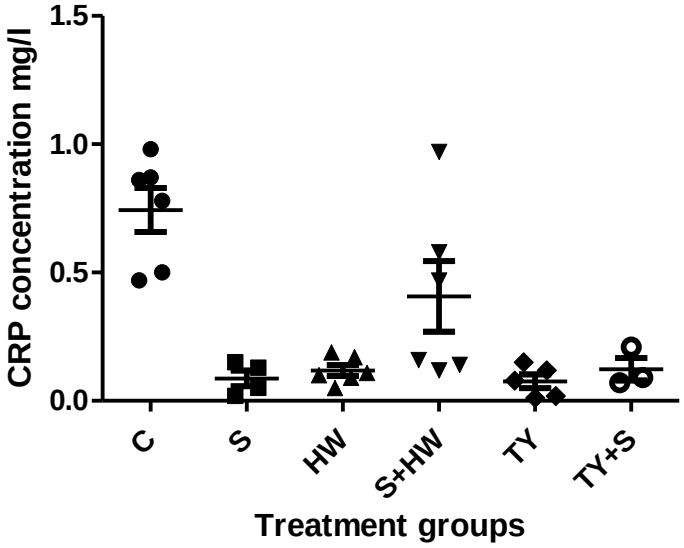


Figure34. Effects of high consumption of crystallize sugar , hot water and traditional yeast on CRP in mice.

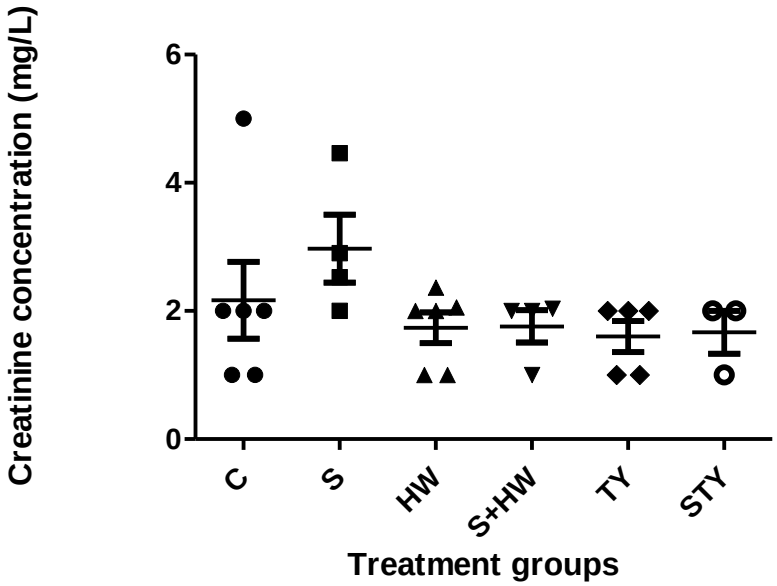


Figure 35. Effects of high consumption of crystallize sugar, hot water and traditional yeast on creatinine in mice.

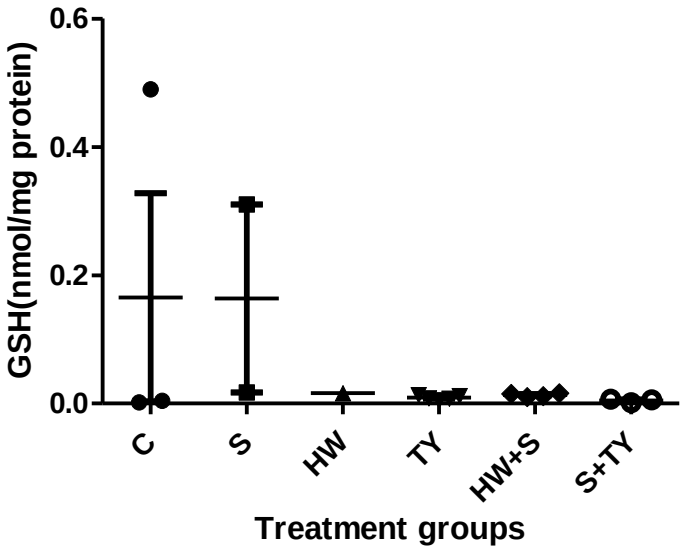


Figure36. Effect of high consumption of crystallize sugar , hot water and traditional yeast on GSH in mice.

1.8-ASAT and ALAT

The data showed that there is a difference significantly between groups in the levels ofthe liver enzyme ASAT $P<0.05$.

The turkey test demonstrated that ASAT is decreased significantly in animal treatedwith hot water (195.05UI/L±39.02) and group treated of traditional yeast(110.74UI/L±36.57) significantly when compared to the control group P<0.05.For the second enzyme, the ALAT there is a difference between groups (C) (144.8UI/L±107.98) (S) (46.55 UI/L±15.25) (HW) (53.16 UI/L±20.83) (S+HW)(41.10UI/L±13.70) (TY) (44.07 UI/L±11.29)(TY+S)(129.18 UI/L±11.67)but not significantly P>0.05 **(Figure37,38).**

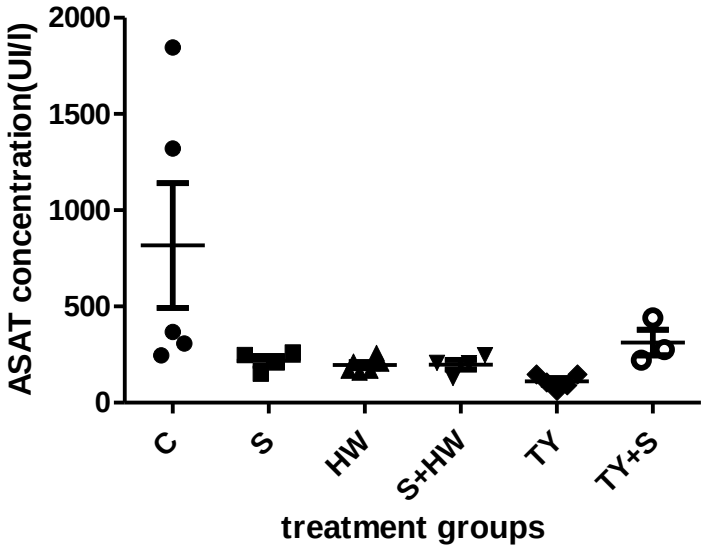


Figure37 . Effects of high consumption of crystallize sugar, hot water and traditional yeast on ASAT in mice.

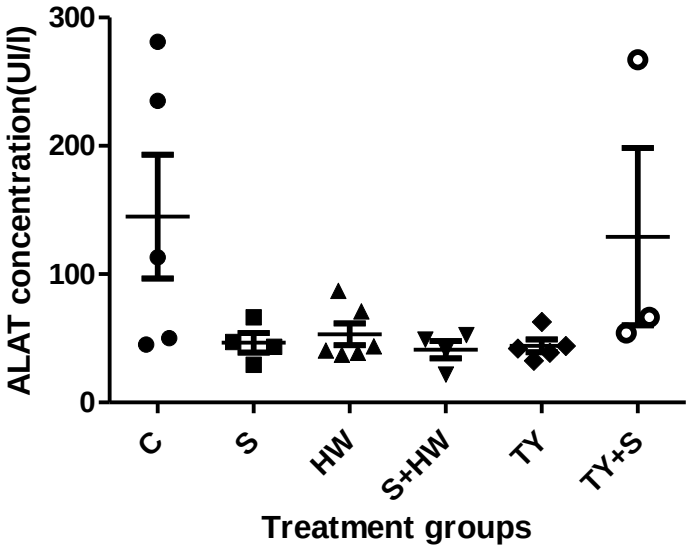


Figure 38. Effects of high consumption of crystallize sugar, hot water and traditional yeast on ALAT in mice.

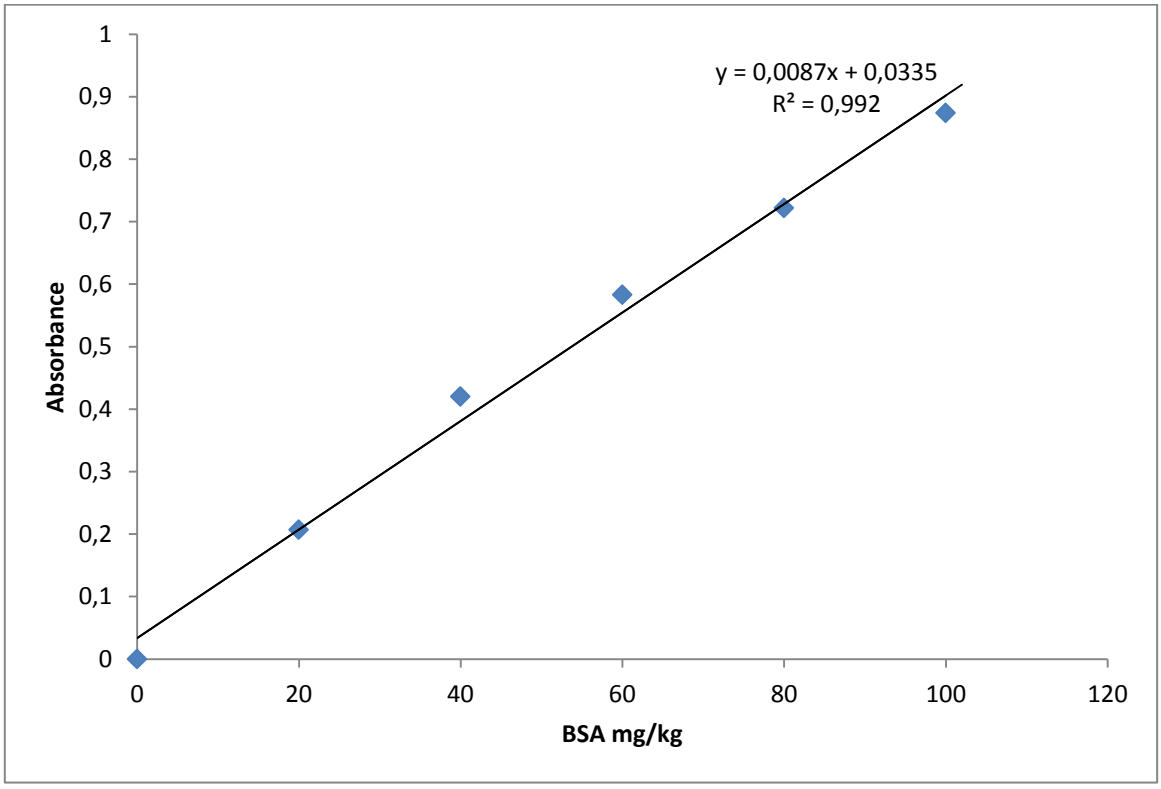


Figure39. Calibration graph.

1.9-Histological sections

Histological investigation showed that the group of mice fed with high crystallize sugar has some lesion on the aorta this was observed through the desquamation of endothelium and the formation of oval nucleus**(Figure41).** In the groups, control , hot water and yeast we have observed that the aorta was intact, the muscular cell nucleus are spindle in chape**(Figure 40,42,43,44).**

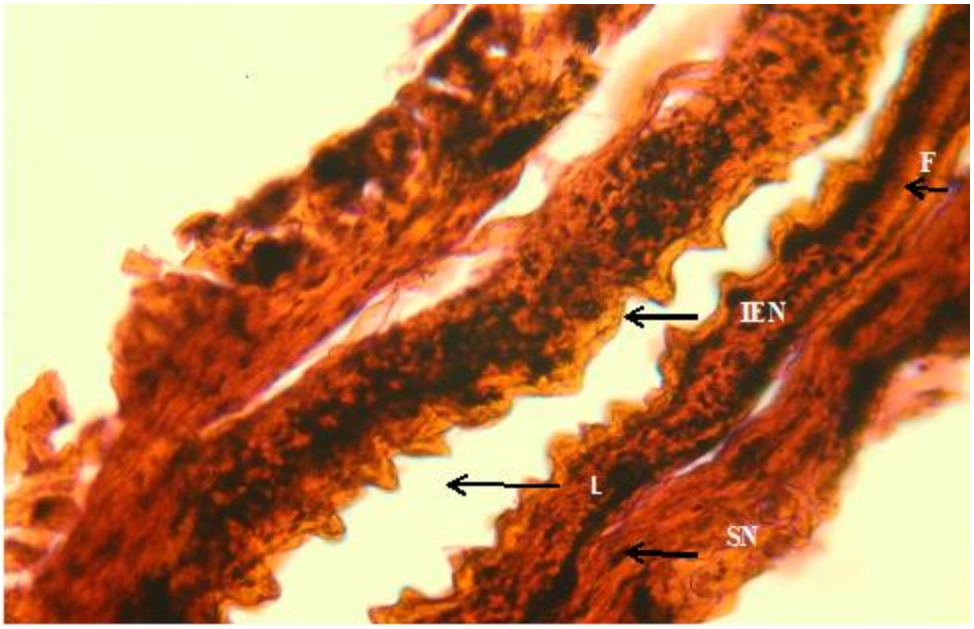


Figure 40. Histological section of the aorta in group control during 21 days .Heamatoxylineosin (*100).

L : lumen , IEN: intact endothelium, EF: elastic fiber , SN: spindle nucleus.

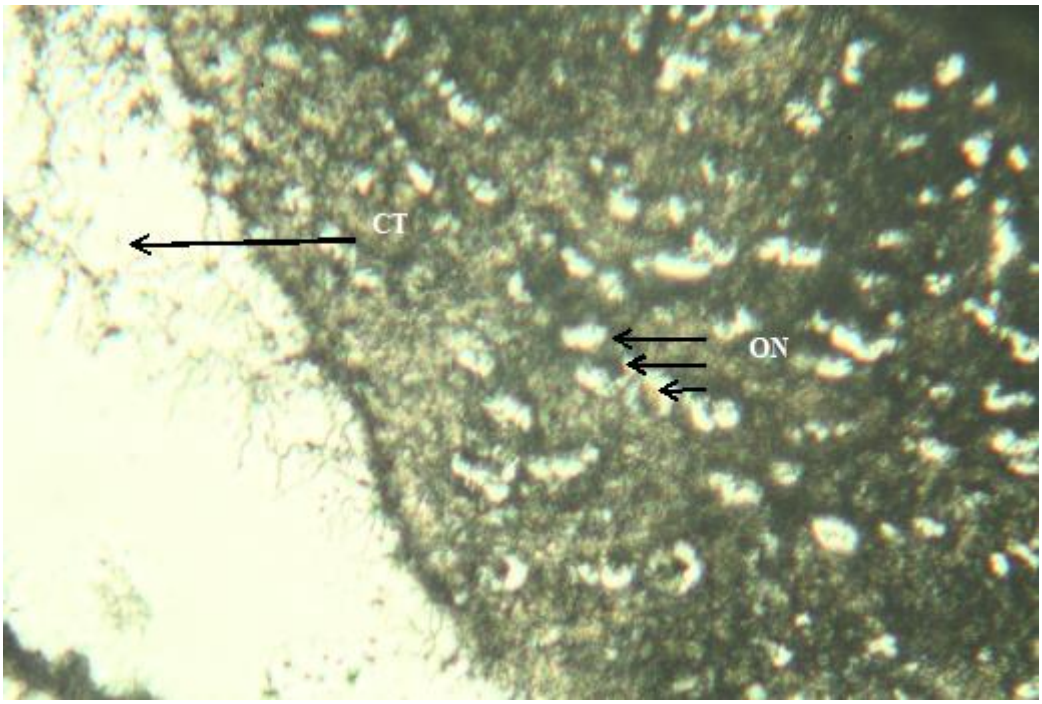


Figure 41. Histological section of the aorta in group fed with crystallize sugar during 21 days.Heamatoxylin eosin (*100).

CT: connective tissue, ON : oval nucleus.

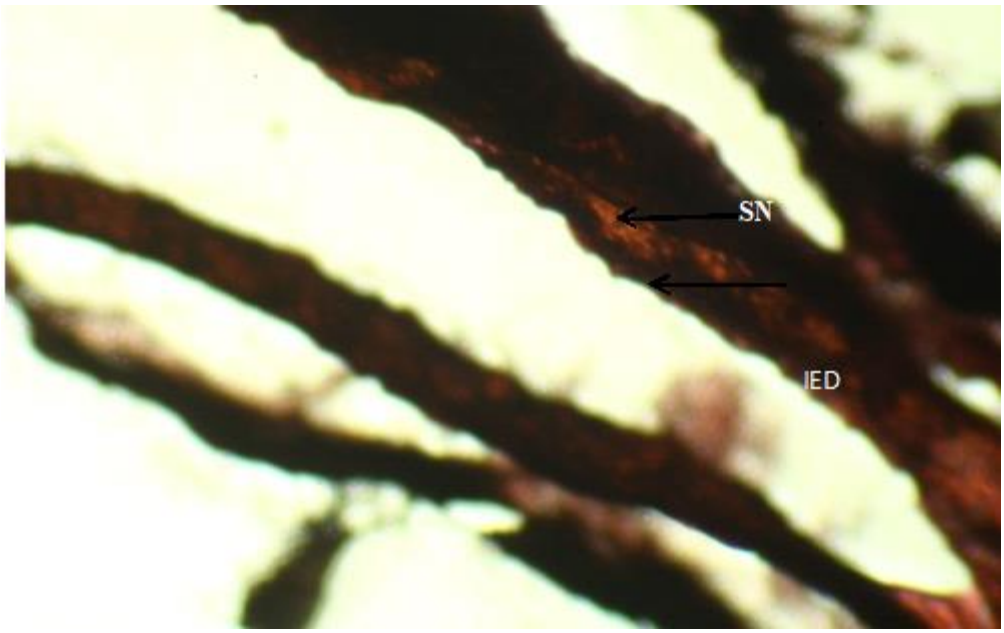


Figure 42. Histological section of the aorta in group treated with hot water during 21 days.Hematoxylin eosin (*100).

SN :spindle nucleus , IED : intact endothelium.

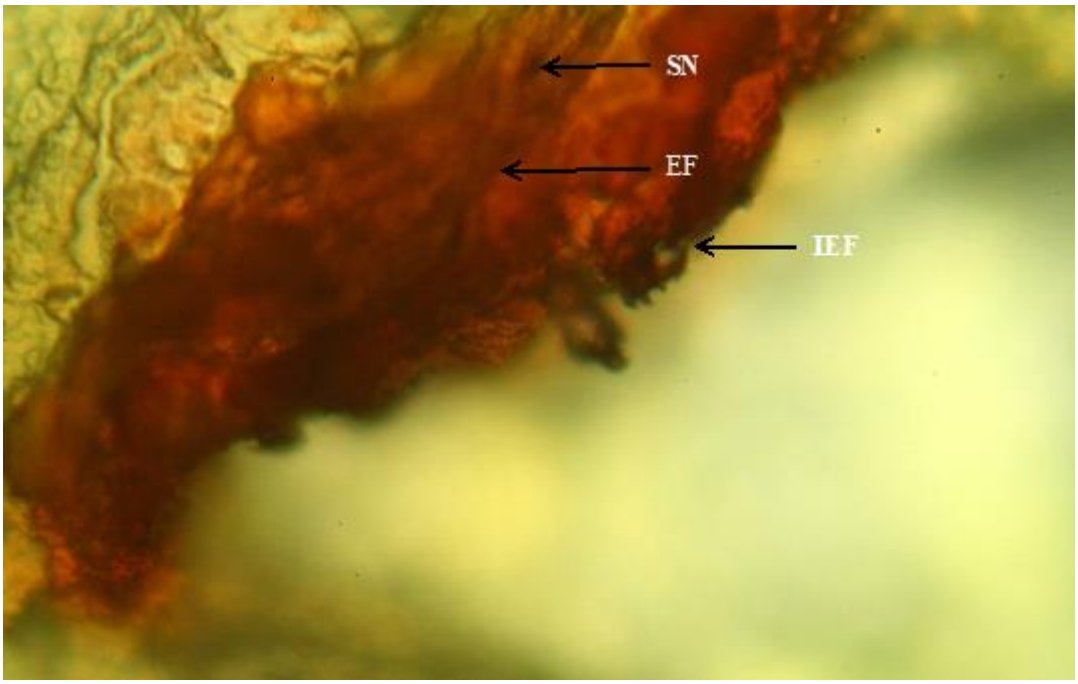


Figure 43. Histological section of the aorta in group treated with traditional yeast during 21 days .Heamatoxylin eosin (*100).

SN :spindle nucleus, IED : intact endothelium, EF :elastic fiber.

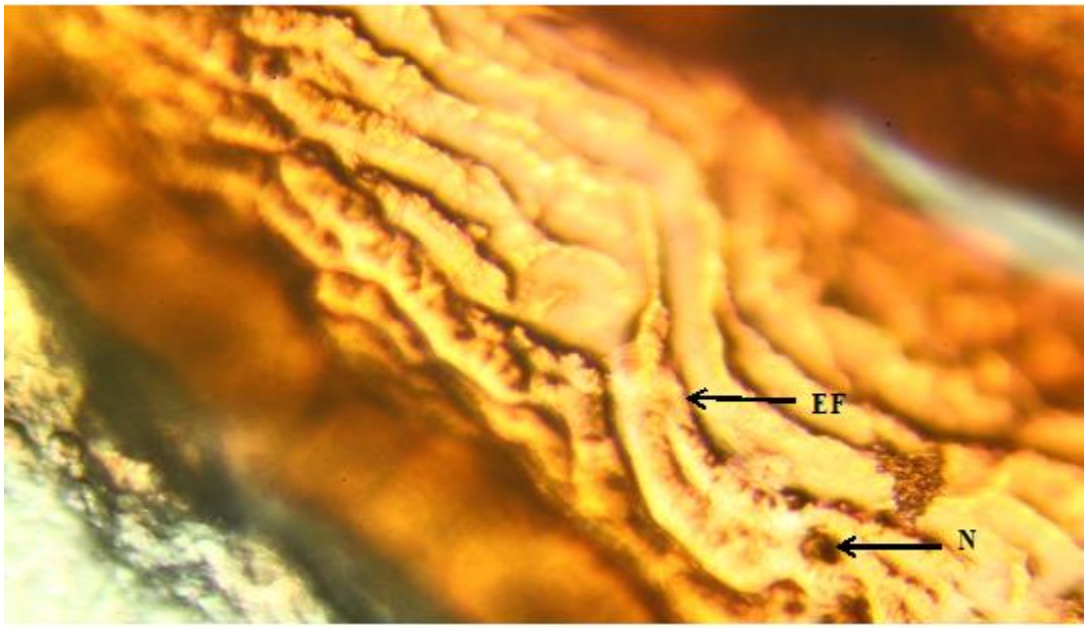


Figure 44. Histological section of the aorta in group treated with traditional yeast during 21 days .Heamatoxylin eosin (*100).

EF : elastic fiber ,N : nucleus

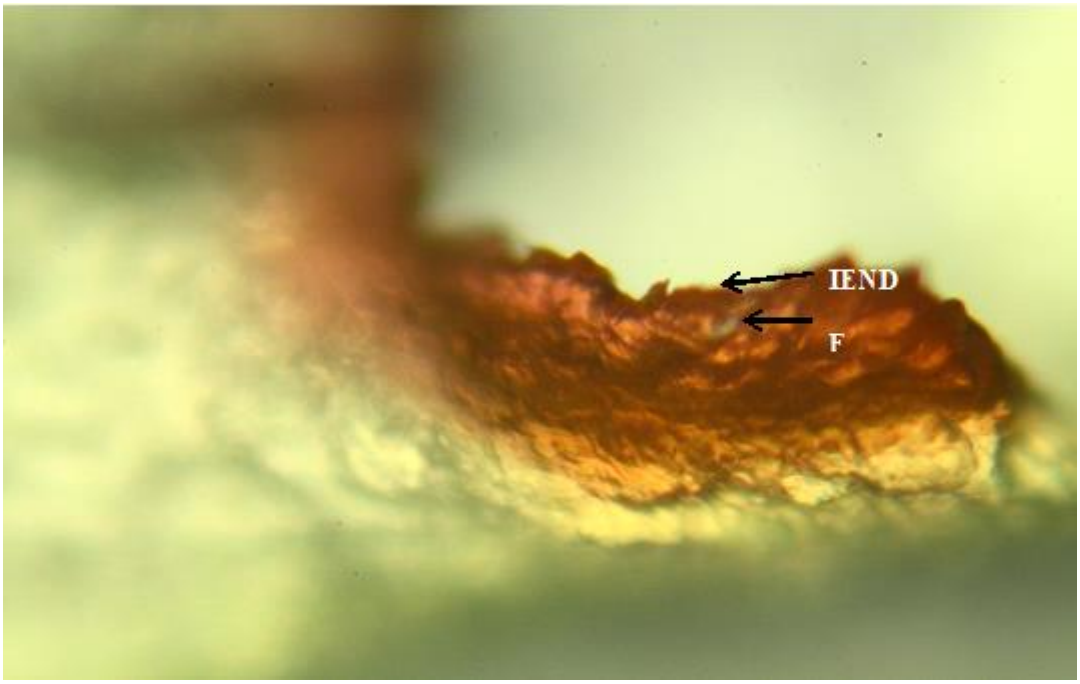


Figure 45. Histological section of the aorta in group fed with crystallize sugar and treated with traditional yeast during 21 days .Heamatoxylin eosin (*40).

IEND : intact endothelium , F: fenestration.

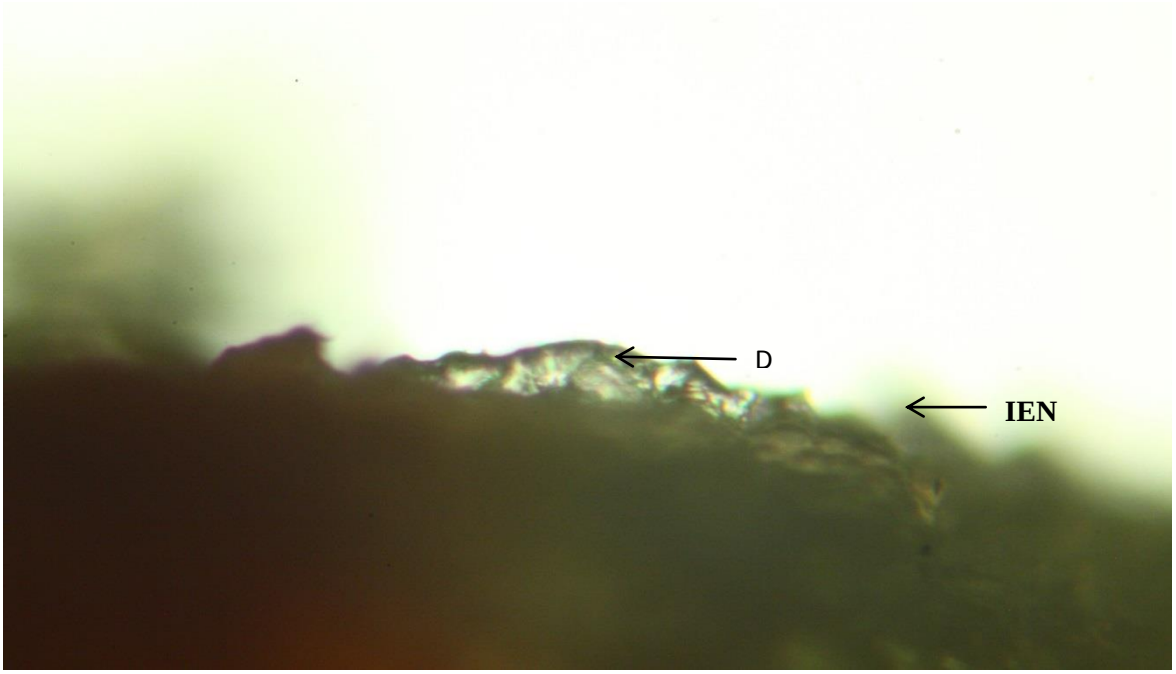


Figure 46. Histological section of the aorta in group fed with crystallize sugar and treated with hot water during 21 days .Heamatoxylin eosin (*100).

D : desquamation , IEND : Intact endothelium.

II-Discussion

Much remains unknown about the role of added sugar in relation to cardiovascular disease

(CVD) and the relative contributions of sugar-sweetened beverages (SSB) or artificiallysweetened beverages (ASB) to CVD risk **(Yang et al., 2022).**

Hyperglycemia has become a common disorder that can lead to various complications.

High blood sugar is clearly associated with the development of cardiovascular disease,

especially in diabetics. The aim of our research is to clarify the effects of a diet high in

crystallized sugar on some biochemical parameters (CRP, Total Cholesterol, Triglyceride,

HDL-C, LDL-c and blood sugar ,creatinine) and on the histological structure of the aorta in miceand to examine the therapeutic effect of hot water and Traditional yeast on the abnormalitiescaused by the high-crystallized sugar diet.

In our research we detected that the weight of mice are slightly increased in group fed with refined crystallize sugar. This result is in agreement with the work of Abderrahmane et al .(2022) who detected an increase in the weight of animals fed with refined crystallize sugar. For instance we have detected an increase of weight in the group treated with hot water. Our result is not agrees with the work of Abderrahmane et al .(2022) who reported that the weight in group of mice is decreased in the group of animals treated with hot water during 21 days of treatment.

Also the weight of mice is increased in group of mice fed with high refined sugar and treated with hot water. Our result is agrees with those of Abderrahmane et al .(2022) who reported that the weight of animal is slightly increased in the group administered with Crystallize sugar and treated with hot water.

The quantity of diet consumed by mice is increased in the groups administered with refined crystallize sugar, treated with hot water, and control group. Same results are obtained by Abderrahmane et al .(2022) who treated animals with crystallize sugar and hot water. We have detected that the group fed with refined sugar and treated with hot water is consumed more food. Our result is not agrees with the result of Abderrahmane et al . (2022) who reported that animals fed with refined sugar and treated with hot water is consumed less quantity of food during the experimental days.

The quantity of food taken by animals is decreased in group fed with diet rich with traditional yeast.

The concentration of blood sugar is increased in animals fed with refined crystallize sugar when compared to the control group. The high intake of sugar can increase the blood pressure, which is a major risk factor for heart disease. People who eat more sugar are more likely to be overweight, and this is a risk factor for heart disease**. (Lennon .,2023).** Also, a higher percentage of calories from added sugar is associated with significantly increased risk of cardiovascular disease CVD mortality. In addition, regular consumption of sugar-sweetened beverages is associated with elevated CVD mortality **(Yang et al .,2014).**

Our study showed that the treatment with hot water could decrease the concentration of blood glucose when compared to the group treated with sugar but it is higher than the control group . There is a benefit of drinking hot water on the stimulation of insulin which converts the glucose to glycogen in the liver. Our result is agrees with Abderrahmane et al .(2022) who found that the blood sugar is decreased in mice fed with refined sugar and treated with hot water.

We detected in this research , mice administered with refined crystallize sugar (200mg/kg) have shown a decrease in the values of lipids (TG, HDL-C) .Abderrahmane et al . (2022) reported that the levels of TG, HDL-C are increased in mice treated with crystallize sugar (50mg/65kg).(50g/65kg).The concentration of T-CH is increased in group S this result is agree withthe result of Abderrahmane et al.(2022). Low cholesterol levels and high cholesterol

variability were associated with a higher risk of Atrial Fibrillation. On the other hand we

detected an increase in the low density lipoprotein (LDL-C) in group S our result is in

accordance with the previous work of Abderrahmane et al. (2022).

The high density lipoprotein is increased in groupTY and decreased in TYS

The c-reactive protein is decreased in the group fed with refined crystallize sugar and the group treated with hot water . This results are same obtained by Abderrahmane et al .(2022). On the other hand the CRP is decreased in the group treated with yeast.

The creatinine levels are increased in the group fed with refined crystallize sugar and decreased in the groups treated with hot water and traditional yeast .

Findings suggest that in the chronic kidney disease (CKD) population, increased sugar sweetened beverages (SSB) intake was associated with a higher risk of mortality and indicated a stratified association with dose. Plain water and unsweetened coffee/tea might be possible alternatives for SSBs to avert untimely deaths **(Xiao et al. , 2019) .**

From our results we found that the liver enzymes (ASAT) are decreased in groups of the experimental study (SHW, TYand STY) and for ALAT in groups (S,HW,TY).

But the level of ALAT was increased in group of animal fed with refined crystallize sugar and traditional yeast where 3 mice are died before the end of the experiment. The hot water could detoxify the body from the toxin decreasing the liver enzymes in the plasma. But the ALAT is affected by adding sugar and traditional yeast to mice this work is orginaland for this reason more study is needed in this part.

Glutathione (GSH), a naturally occurring thioltripeptide of γ-glutamyl-cysteinyl-glycine, plays a vital role in cellular redox reactions and is involved in the inhibition of melanin synthesis, protection from reactive oxygen species, and cell detoxification **(Lee et al., 2020).** where an increase in the level of prooxidants, notably reactive oxygen species, relative to that of antioxidants in cells and tissues results in “oxidative stress”, which potentially leads to oxidative damage to important biological components such as DNA, proteins, and lipids. The change in the ratio of reduced (GSH) to oxidized glutathione (GSSG) has been reported to be diagnostic of various diseases such as cancers, neurodegenerative diseases, and cardiovascular diseases **(Ngamchuea et al., 2017).**

Our results demonstrated that glutathione reduced was lower in the groups of hot water, traditional yeast, sugar + hot water and sugar +traditional yeast compared to the groups control and sugar. Our results are agree with the work of Abderrahmane et al. (2022) who reported that GSH levels are increased in group of mice fed with crystallize sugar and decreased in groups control and hot water. More analysis needs to prove this results by measuring the glutathione oxidized and the dosage of GSH in the plasma.

Histological investigation showed that the group of mice fed with high refined sugar has some lesion on the aorta this was observed through the desquamation of endothelium and the transformation of nucleus spindle to oval **(Figure.41).** This alteration is due to the high level of low density lipoprotein (LDL-C). In contrast to the groups control, hot water and yeast we have observed that the aorta was intact. **(Figure.40.42.43.44)**

The hot water and yeast are useful for decreasing the LDL-C which is one of the factors of inflammation in cardiovascular diseases.

Conclusion

Conclusion

In this experimentation we evaluate the relationship between the high consumption of crystallize sugar (200 g/65kg/day) during 21 days in an *in vivo* animal and evaluate the protective and preventive effect of hot water at 50°C and traditional yeast (sourdough) on lipids profile, marker of inflammation and structural disorders of aorta.

The current study has shown that food rich in high dose of crystallize sugar caused some metabolic disorders manifested by hyperglycemia and hyperlipedemia (increase in T-cholesterol and LDL-C and decrease in HDL-C) . In addition ,histology observations showed desquamation of the endothelium modification of muscular cell nuclei from spindle shape to oval shape. However , a treatment with hot water at 50°C and traditional yeast was effective in preventing the increase of these metabolic disorders and ameliorated the alerations caused by high intake of crystallize sugar.

Based on the findings of this study our future work can evaluate many topics :

1-evaluate the effect of drinking hot water at 50°C and traditional yeast on blood sugar in human, rats and rabbits.

2-evaluate the effect of drinking hot water at 50°C and traditional yeast in rat aorta induced by high crystallize sugar.

3-evaluate other biomarker of inflammation such as myeloperoxidase.

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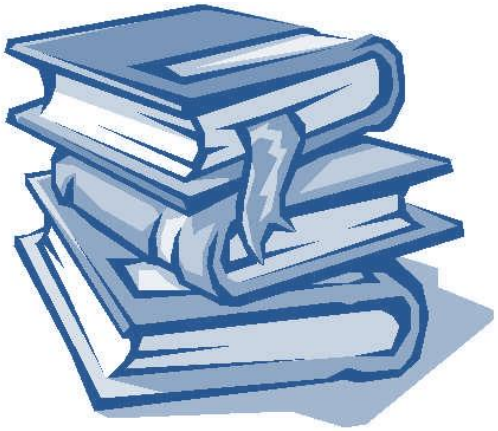

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Summary

Summary

High sugar intake is linked to elevated risk of heart disease and stroke, sugar has negative effects both on the heart and the arteries in several ways.

When we consume excess sugar, the extra calories are stored as triglycerides, and high levels of triglycerides which are a major risk for health disease.

Poor lifestyle factors can interfere in the development of cardiovascular disease, and to avoid these serious consequences, some life style must be taken, such as drinking water, which is a necessary element to prevent dehydration and health problems related to cardiovascular disease, Hot water can help you stay hydrated, and may also help improve digestion, relieving stress and anxiety. It helps to feel warm.

In the present study, we evaluated *in vivo* the interaction of high consumption of refined crystallize sugar , hot water at 50°C and the traditional yeast on aorta during 21 days of experimental study in mice. This was evaluated by using the detection of blood sugar , lipids, CRP, creatinine , GSH concentrations and histological investigations of the aorta .

The findings indicated that using hot water at a temperature of 50°C had the ability to lower the levels of CRP, T-ch levels which help to decrease the inflammation and also we detected a decrease in creatinine, ALAT and ASAT. The consumption of traditional yeast reduces CRP, creatinine and liver enzymes and increase the concentration of HDL-C. We have observed a corrections on some alterations of aorta tissue caused by the consumption of refined crystallize sugar.

We concluded that hot water at a temperature of 50°C and consumption of traditional yeast can be regarded as a natural preventative measure for reducing aortic inflammation.

Keywords :inflammation ,aorta, glutathione reduced ,lipids profile , ASAT , ALAT

Résumé

Un apport élevé en sucre est lié à un risque élevé de maladie cardiaque et d'accident vasculaire cérébral. Le sucre a des effets négatifs à la fois sur le cœur et les artères de plusieurs façons.

Lorsque nous consommons un excès de sucre, les calories supplémentaires sont stockées sous forme de triglycérides, et des niveaux élevés de triglycérides sont un facteur de risque majeur de maladie cardiaque.

De mauvais facteurs liés au mode de vie peuvent interférer dans le développement des maladies cardiovasculaires, et afin d'éviter ces conséquences graves, certains facteurs de santé doivent être pris, comme prendre soin de certaines choses essentielles à la vie, comme l'eau potable, qui est un élément nécessaire pour prévenir la déshydratation et les problèmes de santé liés aux maladies cardiovasculaires, l'eau chaude peut vous aider à rester hydraté et ellepeut également aider à améliorer la digestion, à soulager le stress et l'anxiété et vous aider à vous sentir plus chaud.

Dans notre étude, nous avons évalué *in vivo* l'interaction du sucre cristallisé et de l'eau chaude à 50°C et de la levure traditionnelle sur l'aorte pendant 21 jours expérience chez les souris.
Ceci a été évalué en utilisant la détection de la glycémie, des lipides, de la CRP, de la créatinine, des concentrations de GSH et des investigations histologiques de l'aorte.

Les résultats ont indiqué que l'utilisation d'eau chaude à une température de 50 °C avait la capacité d'abaisser les niveaux de CRP, les niveaux de T-ch qui aident à diminuer l'inflammation et aussi nous avons détecté une diminution de la créatinine, ALAT et ASAT. La consommation de la levure traditionnelle réduit la CRP, la créatinine et les enzymes hépatiques et augmente la concentration de HDL-C. Nous avons observé des corrections sur certaines altérations du tissu aortique causées par la consommation de sucre cristallisé raffiné.
Nous avons conclu que l'eau chaude à une température de 50°C et une consommation de la levure traditionnelle peut être considérée comme une mesure préventive naturelle pour réduire l'inflammation aortique.

Mot clés: inflammation ,aorte, glutahionréduit ,lipids profile , ASAT , ALAT

ملخص

يرتبط تناول كميات كبيرة من السكر بارتفاع مخاطر الإصابة بأمراض القلب والنوبات ، كما أن للسكر آثار سلبية على القلب والشرايين بعدة طرق.

عندما نستهلك السكر بكثرة فانه يتم تخزين السعرات الحرارية الزائدة على شكل دهون ثلاثية ، وتعد المستويات العالية من الدهون الثلاثية عامل خطر رئيسي للإصابة بأمراض القلب.

يمكن أن تتدخل عوامل نمط الحياة غير جيدة في تطور أمراض القلب والأوعية الدموية، ولتفادي هده العواقب الخطيرة لابد من اتخاذ بعض العوامل الصحية مثل الاهتمام ببعض الأمور الضرورية للحياة مثل شرب الماء الذي يعتبر عنصر ضروري لمنع الجفاف والمشاكل الصحية ذات الصلة بأمراض القلب و الأوعية الدموية ، ويمكن أن يساعدك الماء الساخن في الحفاظ .على رطوبة الجسم ، وقد يساعد أيضًا في تحسين الهضم ، وتخفيف التوتر والإجهاد. و يساعد على الشعور بالدفء.

في هذه الدراسة ، قمنا بتقييم أثر استهلاك السكر والماء الساخن عند 50 درجة مئوية مع الخميرة التقليدية على أمراض القلب . والأوعية الدموية خلال 21 يومًا في الفئران باستخدام الكشف عن الجلوكوز في الدم ، الدهون ، الجلوثاثيون المختزل' الكريلتنين'البروتين سي التفاعلي و فحص قطاعات نسيجية على الأورطى.

أشارت النتائج إلى أن استخدام الماء الساخن عند درجة حرارة 50 درجة مئوية له القدرة على تخفيض مستويات بروتين سي التفاعلي و الكولسترول الكلي مما يساعد على تقليل الالتهاب واكتشفنا أيضًا انخفاضًا في الكرياتينين و ALAT و ASAT. استهلاك الخميرة التقليدية تقلل من بروتين سي التفاعلي والكرياتينين وأنزيمات الكبد و تعمل على زيادة تركيز HDL-C وهكذا توصلنا إلى أن الماء الساخن عند درجة حرارة 50 درجة مئوية و استهلاك الخميرة التقليدية يمكن ان يكون واقيا لالتهاب الأورطى.

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الكلمات المفتاحية :الالتهابات'الورطى'الجلوتاثيونالمختزل'الليبيدات' انزيمات كبدية

Annex

Treatment dose calculation

- Sugar given dose (200g/Kg)

200g ⟶ 65000g

X g ⟶ average weight of mice (g)

200g: the amount of sugar consumed by a person weighing 65Kg (65000g).

65000g or 65Kg: weight of person.

X g: the amount of sugar consumed at mice.

- Yeast given dose (50g/Kg)

50g ⟶ 65000g

X g ⟶ average weight of mice (g)

50g: the amount of yeast consumed by a person weighing 65Kg (65000g).

65000g or 65Kg: weight of person.

X g: the amount of yeast consumed by mice.

Preparation of the solutions:

- **Preparation of NaCl 0.9%**

0.9g NaCl⟶ 100 ml distilled water.

- **Preparation of 10% formalin**

10 ml formalin (37%) + 27 ml distilled water.

- **preparation of ethanol**

Ethanol 25%: 25ml ethanol + 71ml distilled water.

Ethanol 60%: 60ml ethanol + 36ml distilled water.

Ethanol 75%: 75ml ethanol + 21ml distilled water.

Ethanol 96%: Used with the same focus.

- **Preparation of DTNB**

0.04g DTNB ⟶ 10ml ethanol (96%).

- **Preparation of TBS**

3.028g Tris + 4.383g NaCl⟶ 500ml distilled water ⟶ pH= 7.4 (modified by HCl).

- **Preparation of Bradford**

0.19g Coomassie Brilliant Blue G-250 ⟶ 50ml ethanol ⟶ 100ml ortophosphoric acid + 850ml distilled water.

- **Preparation sulfosalycilique**

0.25g Sulphosalic acid ⟶ 100ml distilled water.

- **Preparation of Tris EDTA**

6.06g tris + 0.96g EDTA ⟶ 12.5ml distilled water ⟶ pH= 9.6 (modified by HCl.

- **Preparation of alcoholic bouin solution**

1g picric acid ⟶ 45ml ethanol (25%) + 26ml formalin (37%) + 7ml acetic acid ⟶ 22ml distilled water.

- **Preparation of bovine serum albumin (BSA)**

5 mg BSA⟶ 5 ml distilled water

- **Preparation of heamatoxylin**

1 g heamatoxylin⟶ 10 ml distilled water

- **Preparation of eosin**

2 g eosin ⟶ 100ml distilled water

- **Preparation of gelatin**

0.5 g gelatin⟶ 100 ml distilled water

Table 5. Composition of water used in the experimental study.

Composition	**Mg/litre**
Calcium	4.6
Magnesium	3.75
Potasuim	1
Soduim	29
bicarbonates	48.8
Sulfates	10
Chlorures	30
Nitrates	9

Nitrites	0.06
R.S à 105 c°	140
pH	6.87

Table 6. Composition of standart diet (ONAB).

Composition	Amount in g / kg	Percentage %
Corn	620	62
Soja	260	26
Phosphate	16	1,6
Limestone	9	0,9
Cellulose	10	1
Minerals	10	1
Vitamins	10	1

Table7. calibration graph of BSA.

Tube	**1**	**2**	**3**	**4**	**5**	**6**
Distilled water (ml)	100	80	60	40	20	0
BSA (µl)	0	20	40	60	80	100
Bradford(ml)	5	5	5	5	5	5
DO	0	0.207	0.420	0.583	0.722	0.874

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The effect of hot water and traditional yeast on aorta inflammation induced by refined crystallize sugar

Thesispresented for the obtention of the degree of master II

High sugar intake is linked to elevated risk of heart disease and stroke, sugar has negative effects both on the heart and the arteries in several ways.

When we consume excess sugar, the extra calories are stored as triglycerides, and high levels of triglycerides which are a major risk for health disease.

Poor lifestyle factors can interfere in the development of cardiovascular disease, and to avoid these serious consequences, some life style must be taken, such as drinking water, which is a necessary element to prevent dehydration and health problems related to cardiovascular disease, Hot water can help you stay hydrated, and may also help improve digestion, relieving stress and anxiety. It helps to feel warm.

In the present study, we evaluated *in vivo* the interaction of high consumption of refined crystallize sugar , hot water at 50°C and the traditional yeast on aorta during 21 days of experimental study in mice. This was evaluated by using the detection of blood sugar , lipids, CRP, creatinine , GSH concentrations and histological investigations of the aorta .

The findings indicated that using hot water at a temperature of 50°C had the ability to lower the levels of CRP, T-ch levels which help to decrease the inflammation and also we detected a decrease in creatinine, ALAT and ASAT. The consumption of traditional yeast reduces CRP, creatinine and liver enzymes and increase the concentration of HDL-C. We have observed a corrections on some alterations of aorta tissue caused by the consumption of refined crystallize sugar.

We concluded that hot water at a temperature of 50°C and consumption of traditional yeast can be regarded as a natural preventative measure for reducing aortic inflammation.

Keywords : inflammation ,aorta, glutathione reduced ,lipids profile , ASAT , ALAT

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