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# The effect of hot water and traditional yeast on the heart inflammation induced by refined crystallize sugar

Presented by**:** Boughachiche Zina
Bouzid Amira
Derouiche Maroua

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**Examination board:**

**Chairman : CHETTOUME Aziez** (Pr. UFM Constantine 1).
**Supervisor : ZERIZER Sakina** (Pr. UFM Constantine 1).
**Examinator : HADAD Souad** (MAA. UFM Constantine 1).

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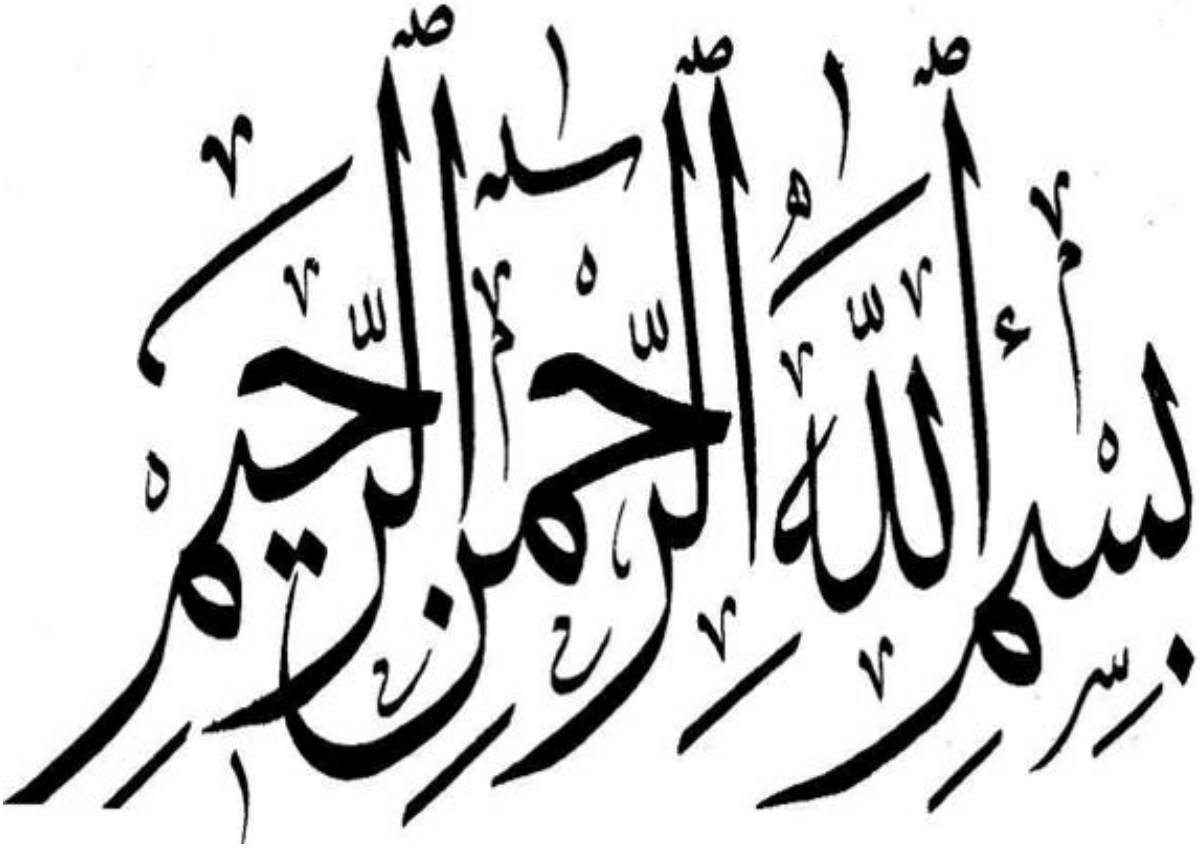
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*To the one I prefer over my self, who set me on the path of life, made me calm down, took care of me until I became an adult (dear mother,* ***Badia****), may allah bless her soul.*

*We walk the paths of life, and the one who controls our fats in every path we take remains the one with a good face and good deeds. He was primarily credited with getting me higher education. He did not stingy on me throughout his life (dear father,* ***Abd Alhak****), may allah prolong his life.*

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*To the symbol of love and healing balm, with a white heart "Dear Mama".*

*For the kind hearts and innocent souls of the winds of my life, my "brothers" and "sisters" and my support in life, "Sami".*

*To the youngest chick in my family, my niece Tasneem.*

*To all my family and friends I dedicate this humble work.*

***Maroua***

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## List of abbreviations

**AGP** acid glyco protein

**ATP** adenosine triphosphate

**AV** atrioventricular

**C** control

**CCL3** chemokine ligand 3

**CCR7** chemokine receptor 7

**CRP** c-reactive protein

**DCs** dendritic cells

**DHF** diastolic heart failure

**DP** degree of polymerization

**ECs** endothelial cells

**EMP** embden-meyerhof-parnas

**ESR** erythrocyte sedimentation rate

**FC** crystallized fragment

**FCɣR** crystallized factor gamma receptor

**HDL** high-density lipoprotein

**HW** hot water

**IBD** inflammatory bowel disease

**ICAM** intercellular adhesion molecule-1

**IFN ɣ** interferon gamma

**IL- α** interleukin alpha

**IL- β** interleukin beta

**IL-1 β** interleukin 1beta

**IL-1** interleukin1

**LA** left atrium

**LAD** left anterior descending artery

**LCx** left circumflex artery

**LDL** low-density lipoprotein

**LV** left ventricle

**mCRP** monomeric c-reactive protein

**MI** myocardial infarction

**MMPs** matrix metallo protéinases

**$NAD^+$** nicotinamide adenine dinucleotide

**$NADH^+$** nicotinamide adenine dinucleotidehydrogen

**NAFLD** non alcoholic fatty liver disease

**NETs** neutrophil extracellular traps

**NF-κB** 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

**PDA** posterior descending artery

**PGs** prostaglandins

**PMNs** pollymorphonuclear cells

**PRRs** pathogen recognition receptors

**RA** right atrium

**RCA** right coronary artery

**ROS** reactive oxygen species

**RV** right ventricle

**S** sugar

**SA** sinoatrial

**SHF** systolic heart failure

**SMC** 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

**TY** traditional yeast

**VAT** visceral adipose tissue

**VCAM** vascular cell adhesion molecule

**VCAM-1** vascular endothelial cell adhesion molecular-1

**VEGEF** vascular endothelial growth factor

**VSMC** vascular smooth muscle cells

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# Introduction

Over the span of a few decades the lifestyles of modern humans have changed drastically from physically demanding lives and agrarian diets to physically inactive routines and chronic over-consumption of calorie-dense beverages and processed foods **(Bhardwaj et al., 2016)**.

Sugar and sweet consumption have been popular and intrinsic to culture, traditions, and religion from ancient times. Along with decreasing physical activity, the increasing trend of sugar consumption assumes significance in view of the high tendency to develop insulin resistance, abdominal adiposity, and hepatic steatosis, and the increasing "epidemic" of type 2 diabetes (T2DM) and cardiovascular diseases **(Gulati and Misra, 2014)**.

Higher intake of sugar was associated with increased CVD in cross-country comparisons. Women who consume diets with a high glycemic load (increased blood glucose excursions associated with intake of sweets or highly processed starches and sweets) have an increased coronary heart disease (CHD) risk **(Howard and Wylie-Rosett, 2002)**.

Dietary sugars and mixed processed foods may be a key factor leading to the occurrence and aggravation of inflammation **(Ma et al., 2022)**. Large amounts of glucose may lead to impaired immune system function **(Xi et al., 2015)**. Therefore, high glucose induces a series of complications by suppressing the effective adaptive immune response generated by macrophages and T cells **(Ma et al., 2022)**.

Atherosclerosis is a disease of the vessels consisting of both degenerative and regenerative processes that initially affect the intima and at a later stage the media at the bifurcations of the major arteries **(Tegoset al., 2001)**. It is a disease of chronic inflammation, which ultimately results in tissue damage and fibrosis. Multiple risk factors for atherosclerosis have been defined including smoking, hypercholesterolemia, hypertension, hyperglycemia and genetic factors, and cardiovascular disease (CVD) can develop in the absence of such risk factors **(O'connoret al., 2001)**.

Hydrotherapy is one of the non-pharmacological therapies that aim to help the process of removing all the poisons in the body including excess blood glucose therefore it can reduce blood glucose levels **(Siswanti et al., 2021)**. Water intake in non-pregnant, non-lactating animals is well regulated in order to maintain body fluid homeostasis **(Andersson, 1978)**.

During lactation, water is needed for milk secretion, which places extra strain on the fluid-regulatory systems **(McDowell et al., 1969)**. Drinking cold water excessively develop hyponatraemia **(Olsson and Dahlborn, 1989)**. The practice of drinking warm water have benefits over the cold water drinking practice. It is beneficial for maintaining normal health **(Joshi, 2015)**.

People have been baking bread with yeast for thousands of years. It is the natural leavening that gives bread its flavor **(McGruther, 2022)**. With the progress and advent of science and technology in nutrition, sourdough fermentation is now known to possess many desirable attributes in terms of health benefits. It has become the focus of attention and practice in modern healthy eating lifestyles when linked to the secret of good health. The sourdough starter is an excellent habitat where natural and wild yeast plus beneficial bacteria grow by ingesting only water and flour **(Lau et al., 2021)**.

In the present study, our objectives were to:

- Evaluate the effect of sugar, traditional yeast and hot water on the weight and consumed food of mice.
- 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.
- Evaluate the benefits of hot water at 50°c and traditional yeast on some biochemical parameteres.
- Determinate histological section of heart tissue.

# Chapter I: sugar and inflammation

# Sugar and inflammation

## I. Sugar

### I. 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 su crose, a crystalline tabletop and industrial sweetener used in foods and beverages **(Zaitoun 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 **(Zaitoun et al., 2018)**.

**Carbohydrates**

Carbohydrates are the main source of energy that the human body ingests **(Asif et al., 2011)**.Carbohydrates are moleculesconsistingmainly of three basic elements ofcarbon, oxygen and hydrogenwith the empirical formula (CH2O) **(Aldairi, 2020)**.

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)**.

## I. 2. Chemical structure of carbohydrates types

Structurally they are polyfunctional 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 are classified into monosaccharides, disaccharides, oligosaccharides, polysaccharides (Figure 01) **(Asif et al., 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)**.

### I.2. 1. Simple carbohydrates

#### 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 02).

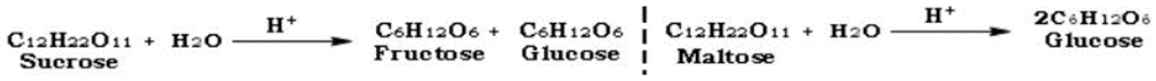
Sugars are also named according to their number of carbons, some of the most common types are trioses (three carbons), pentos (five carbons), and hexoses (six carbons) **(Mondal, 2017)**.

#### 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 03) **(Howard and Wylie-Rosett, 2002)**.

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




### I.2. 2. Complex carbohydrates

#### 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 includeraffinose, stachynose and verbascose (Figure 04) **(Ahnen et al., 2020)**.

#### Polysaccharides

Polysaccharides are essential macromolecules which almost exist in all living forms **(Mohammed et 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 (Figure 05) **(Mondal, 2017)**.

## I.3. 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 and Hyvönen et al., 1985)**.

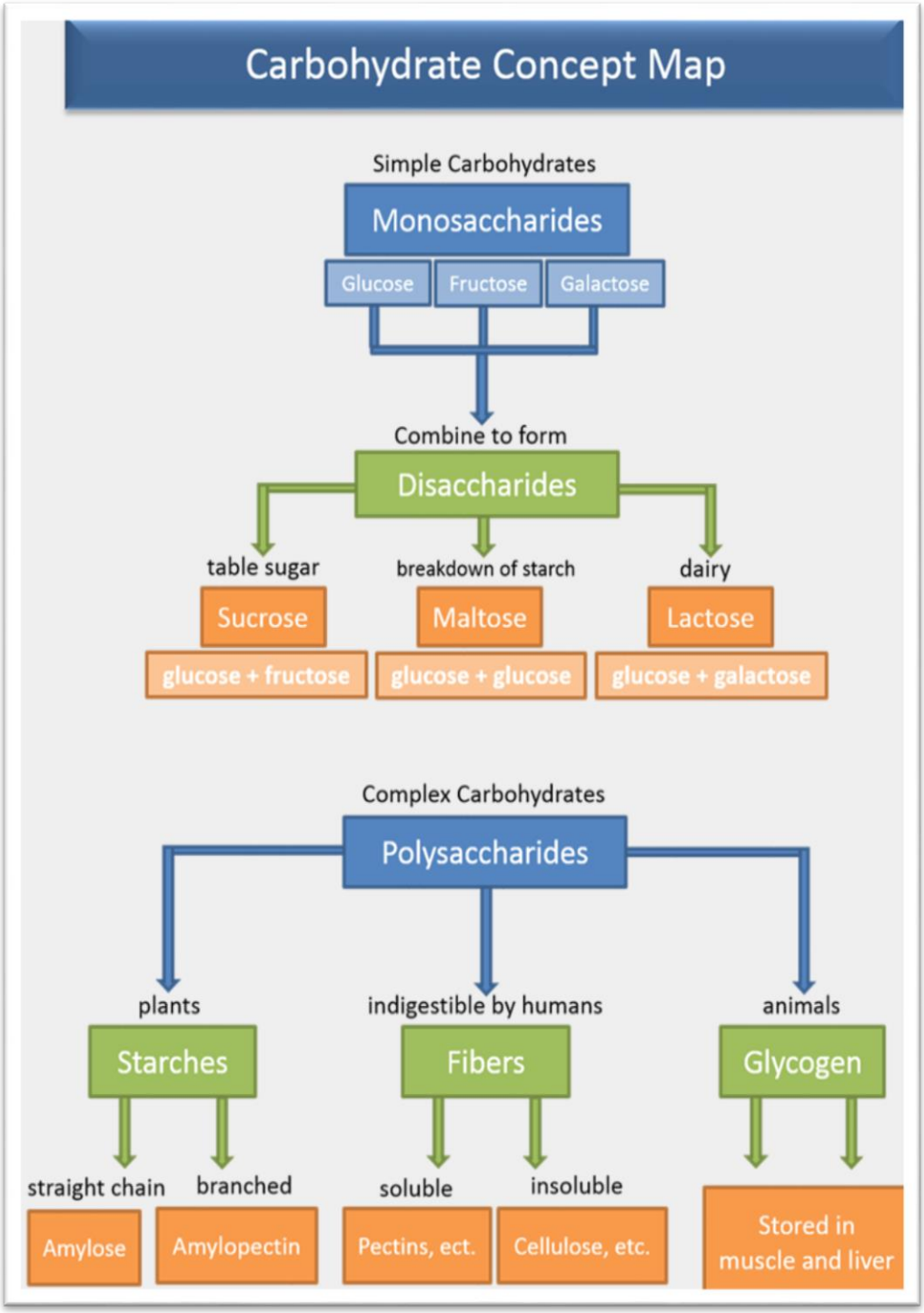



**Figure 01:** carbohydrate concept map (Site web 01).

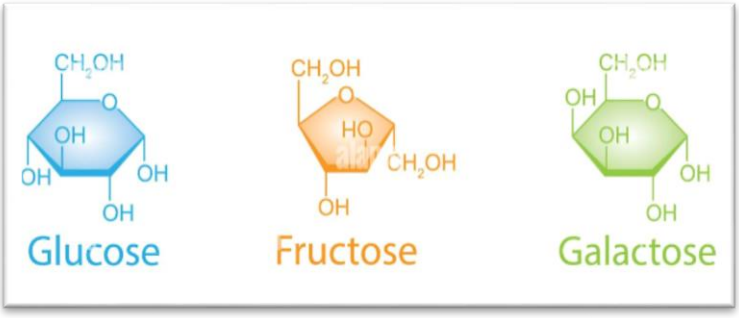



**Figure 02:** linear and ring structures of three common monosaccharides. All have the same molecular formula (C6H12O6), but they have different structures (red) and are therefore isomers of each other (Site web 2).

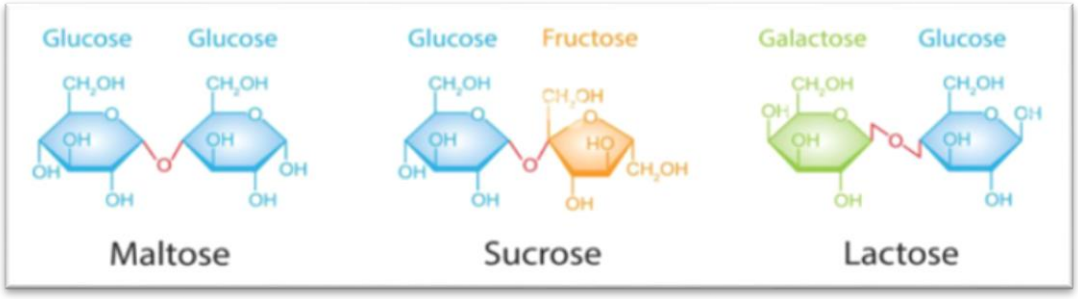



**Figure 03:** structures of the three common disaccharides. All contain glucose as one of their subunits, the difference between the three is the second subunit (Site web3).

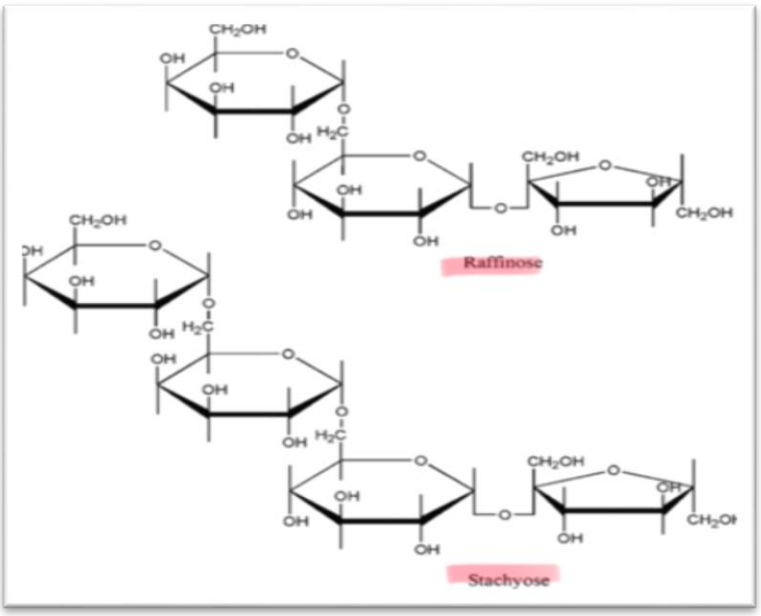



**Figure 04:** oligosaccharides, liaisons glycosidiques, 8-10 monosaccharides (Site web 4).

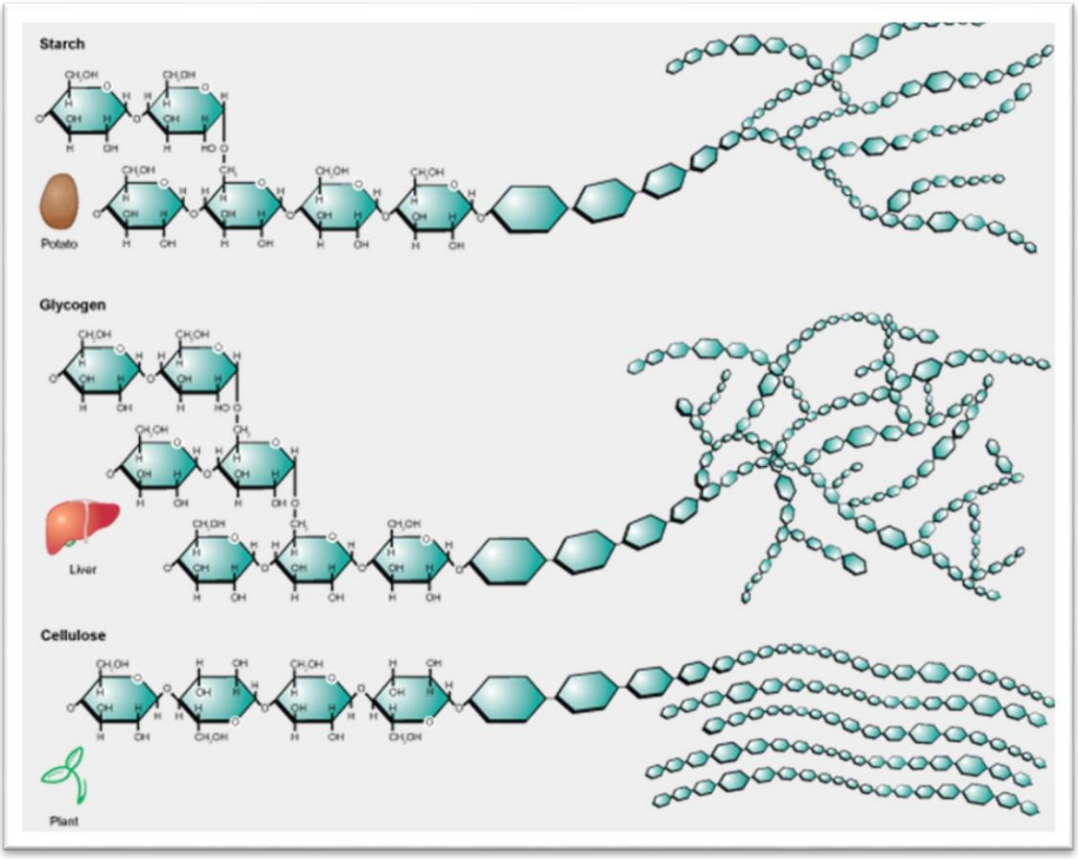



**Figure 05:** structures of the three common polysaccharide: starch, glycogen, cellulose (site web 5).

## I. 4. 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)**.

## II. Inflammation

### II. 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 06) **(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)**.

### II. 2. 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 et al., 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 01).

**Table 01:** inflammatory markers.

| Marker | Application |
|---|---|
| **C-reactiveprotein (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)**. |
| **Serumamyloid 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.<br><br>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.<br><br>Cytokines which have proinflammatory effects include interferon IFN$\gamma$, interleukin IL-17, IL-1$\beta$, and tumor necrosis factor TNF$\alpha$, and those with anti-inflammatory effects include IL-10, IL-4, and IL-1 **(Monastero and Pentyala, 2017)**. |

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

## II. 3. 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-Kinsky, 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:

### II. 3. 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 **(Sherwoodand Toliver-Kinsky, 2004)**.

Activation of members of the selectin 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)**.

### II. 3. 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, have the ability to chemically attract specific groups of leukocytes. Activated neutrophils increase their level of Fc receptor expression allowing the increased uptake and phagocytosis of pathogens **(Thacker, 2006)**.

### II. 3. 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)**.

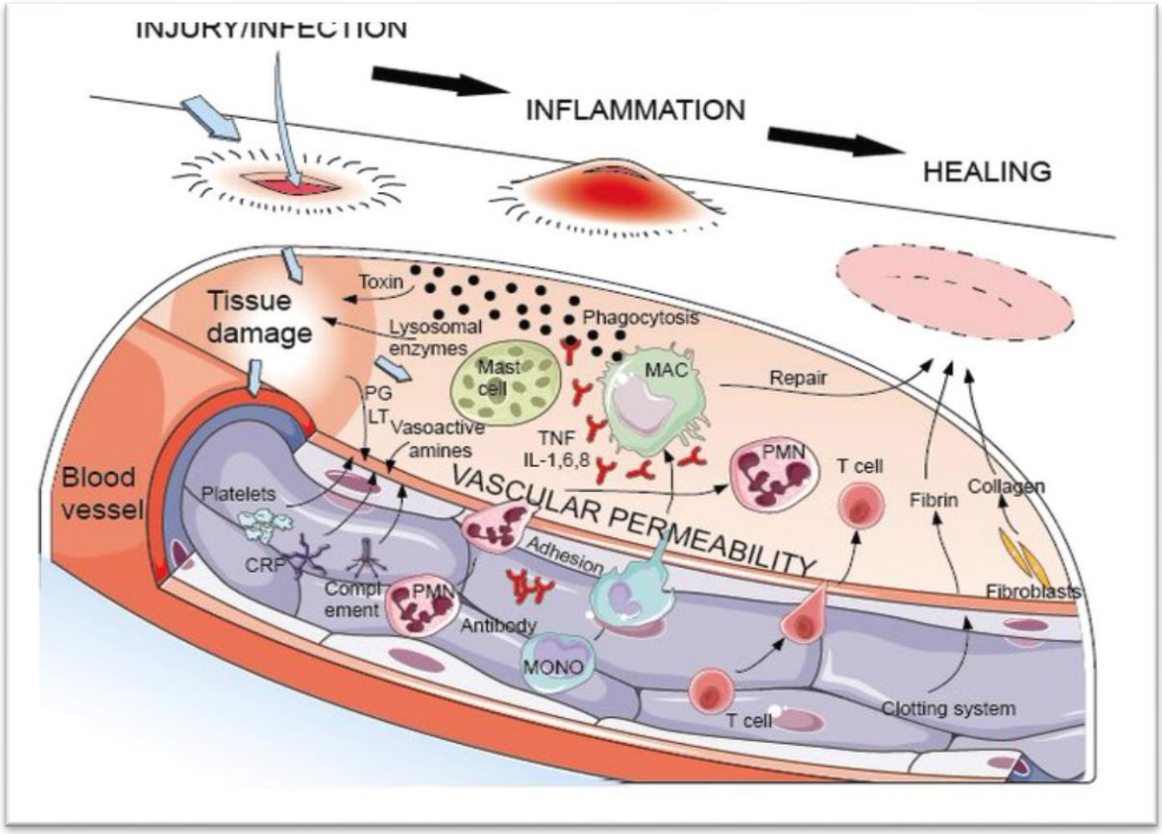


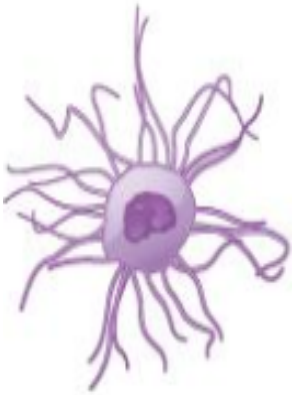

**Figure 06:** showing signs of inflammation and the stages of response (site web 6).

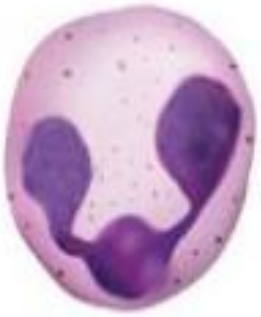
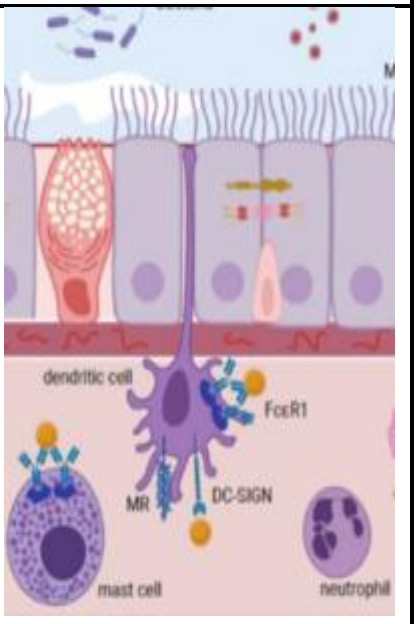
### II. 3. 4. Cells of inflammation

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 dendrotic cells.

**Table 02:** 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.<br><br>Secrete numerous vasoactive and pro-inflammatory mediators such as histamine, serotonin, TNF, kinins and proteases stored in secretory granules **(Theoharides et al., 2012)**.<br><br>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)**.<br><br>It has role in innate or acquired immunity, bacterial infections, as well as in autoimmunity.<br><br>Superactivate T cells through TNF **(Theoharides 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.<br><br>**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 **(ItalianiandBoraschi, 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.<br><br>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 nonself-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 TNFα **(Rosales, 2018) (Wright et al., 2010)**. |  |
| **Epithelial cells** | Epithelial cells derived from airway, intestinal and ocular mucosal sites actively participate during inflammatory processes.<br>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.<br>Can play roles as non-professional antigen presenting cells in the recruitment and activation of lymphoid cells **(Enríquez et al., 2008)**. |  |

## II. 4. Types of inflammation

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

### II. 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. Subacute inflammation is the period between acute and chronic inflammation and maylast 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 proinflammatory cytokines, which activate downstream proinflammatorysignalling **(Feehan and Gilroy, 2019)**.

### II. 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 et 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 **(Zhao 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)**.

## II. 5. C-reactive protein

### II. 5. 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 **(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 **(Vermeire et al., 2004)**.

**Nehring et al. (2017)**, 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 fibronect.

### II. 5. 2. Structure of C-reactive protein

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. There are five PCh-binding sites, one located on each subunit (Figure 07) **(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 ribonucleoproteins **(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 concanavalinA 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 08) **(Shrivastava et al., 2014)**.

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

### II. 5. 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 phosphocholine 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 upregulatesthe expression of adhesion molecules in endothelial cells (Ecs) that can attract monocytes to the site of injury **(Pfutzner et al., 2010)**.

**Davis et al. (2012)**, reported that CRP increases 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.

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)**.

### II. 5. 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 immunonephelometric techniques and, more recently, automatized immunoluminometry and immunoturbidimetry, 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)**.

### II. 5. 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 (Figur 09) **(Pradhan et al., 2001)**.

pentameric C-reactive protein (pCRP) induces the upregulation of cell adhesion molecules such as intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and E-selectin via NF-k bupregulation **(Thiele et al., 2015)**.

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

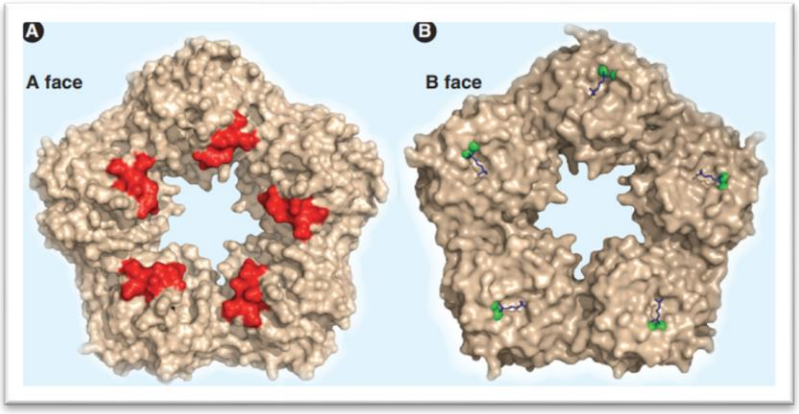



**Figure 07:** pentameric structure of C-reactive protein (CRP). (A) Space - filling model of the A face (receptor and C1q binding) of the CRP pentamer with the ridge helix in red. (B) Spacefilling model of the CRP molecule showing a phosphocholine molecule (blue) with the two calcium molecules (green) located in the binding site of each protomer on the B face (ligand - binding face) **(Peisajovich et al., 2008)**.

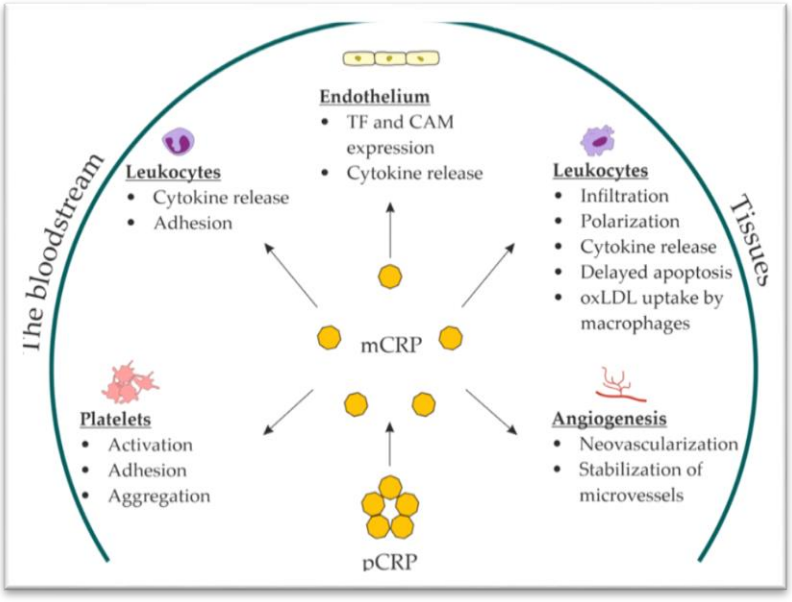



**Figure 08:** proposed roles for mCRP in atherosclerosis. mCRP, monomeric C-reactive protein; pCRP: pentameric C-reactive protein. TF: tissue factor. CAM: cell-adhesion molecules. oxLDL: oxidized low-density lipoproteins **(Melnikovet al., 2023)**.

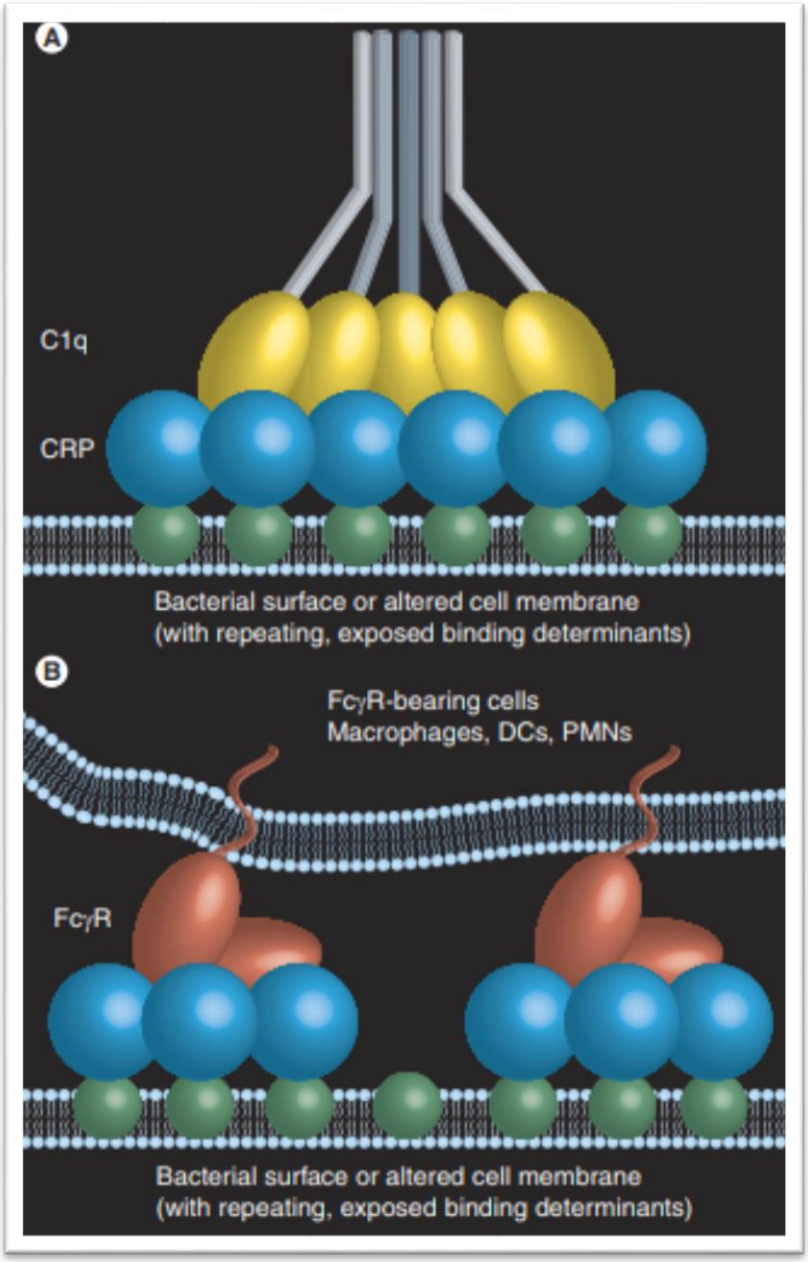



**Figure 09:** CRP bound to bacterial or altered cell surfaces. CRP binds to a surface on its B-face phosphocholine-binding site, leaving the A face exposed. This allows each pentamer to bind either (A) one of the six globular heads of C1q leading to the activation of the classical complement cascade or; (B) FcγR on the surface of macrophages, DCs or PMNs. The type of FcγR helps to determine the downstream effect of this binding. CRP: C-reactive protein; DC: Dendritic cell; FcR: Fcγ receptor; PMN: Polymorphonuclear cell (neutrophil) **(Peisajovich et al., 2008)**.

# Chapter II: sugar and cardiovascular disease

# Sugar and cardiovascular disease

## II. 1. The anatomy of the heart

The heart is a unique organ in the human body. It is a muscle pump with independent electrical activity that is governed by central innervation. Unlike other organs, such as the digestive tract, its cells are not subject to repair or division. The heart is situated in the midline of the mediastinal cavity, somewhat to the left turned posteriorly, with the right ventricle occupying the majority of the anterior surface (Figure 10) **(Bakose et al., 2023)**.

The heart beats around 100,000 times a day, pumping approximately 8 pints of blood throughout the body 24/7. This delivers oxygen- and nutrient-rich blood to tissues and organs and carries away waste **(Kohli, 2020)**.

The heart sends deoxygenated blood to the lungs, where the blood loads up with oxygen and unloads carbon dioxide, a waste product of metabolism.

Together, the heart, and blood vessels -arteries, capillaries, and veins -make up the circulatory system **(Kohli, 2020)**.

### II. 1. A. Chambre of the heart

The heart consists of four chambers

**The atria:** these are the two upper chambers, which receive blood.

**The ventricles:** these are the two lower chambers, which discharge blood. A wall of tissue called the septum separates the left and right atria and the left and right ventricle. Valves separate the atria from the ventricles **(Kohli, 2020)**.

There are 4 valves that maintain blood flow, these valves are located between the atria and the ventricles and in the arteries, emptying blood into the ventricle **(Charitos and Sievers, 2013)**.

#### A.1. Left and right sides

The left and right sides of the heart work in unison. The atria and ventricles contract and relax in turn, producing a rhythmic heartbeat **(Kohli, 2020)**.

#### A.1.1. Right side

The right side of the heart receives deoxygenated blood and sends it to the lungs.

The right atrium receives deoxygenated blood from the body through veins called the superior and inferior vena cava. These are the largest veins in the body. The right atrium contracts, and blood passes to the right ventricle. Once the right ventricle is full, it contracts and pumps the blood to the lungs via the pulmonary artery. In the lungs, the blood picks up oxygen and offloads carbon dioxide **(Kohli, 2020)**.

### A.1.2. Left side

The left side of the heart receives blood from the lungs and pumps it to the rest of the body. Newly oxygenated blood returns to the left atrium via the pulmonary veins. The left atrium contracts, pushing the blood into the left ventricle. Once the left ventricle is full, it contracts and pushes the blood back out to the body via the aorta **(Kohli, 2020)**.

### II. 1. B. Coronary arteries and veins

Coronaryarteries and veins, lymphatic vessels, and nerves run below the epicardium. The endocardium is composed of the endothelium and the subendothelial connective tissue layer. The subendocardium is found between the endocardium and myocardium and contains the impulse-conducting system **(Arackal and Alsayouri, 2019)**.

The impulse conducting system has specialized cardiac cells for the conduction of electrical impulses throughout the heart. Electrical impulses initiate at the sinoatrial (SA) node, situated at the junction of the superior vena cava and right atrium. These impulses travel throughout the atria until it reaches the atrioventricular (AV) node, located between the interatrial and interventricular septum. As the fibers travel inferiorly, it penetrates the central fibrous body of the cardiac skeleton to form the bundle of His. These fibers are the Purkinje fibers after they divide within the interventricular septum and branch into the ventricles **(Arackal and Alsayouri, 2019)**.

### B. 1. Coronary arteries

Because of its heavy work load, your heart requires a particularly rich blood supply. At rest, the blood flow through the coronary arteries averages about 225ml a minute.

The coronary arteries branch off from the base of the aorta just above the aortic valve. They run along the surface of the heart, encircling the top and branching toward the bottom like a crown.

The left coronary artery carries blood to the front, top, and part of the back side of the left ventricle. The right coronary artery supplies most of the right ventricle and also a portion of the undersurface and back of the left ventricle **(Gersh, 2000)**.

The left main coronary artery divides into the anterior descending artery, which carries blood down the front of the heart to both ventricles, and the circumflex artery, which winds around the back of the heart to nourish that portion of the left ventricle and left atrium.

The right coronary artery curves around the front of the heart between the right atrium and right ventricle, sending branches, the marginal arteries, along the front to bring blood to the right ventricle. Blood vessels extend through heart muscle to supply all layers of the muscle **(Gersh, 2000)**.

**B.2. Coronary arterial dominance**

Coronary arterial dominance is defined by the vessel which gives rise to the posterior descending artery (PDA), which supplies the myocardium of the inferior third of the interventricular septum **(Rogalskyi, 2022)**.

Most hearts (80-85%) are right dominant where the PDA is supplied by the right coronary artery (RCA). The remaining 15-20% of hearts are roughly equally divided between left dominant (~10%) and codominant (~20%). The strict definition of codominance can vary depending on which modality one uses to assess the coronary arteries (coronary angiography) but is not overly important. In left dominant hearts the PDA is supplied by the left circumflex artery (LCx) wrapping around the left atrioventricular groove, or less commonly the left anterior descending artery (LAD) coursing around the apex of the heart. In a codominant heart a single or duplicated PDA is supplied by branches of both the RCA and the LAD or LCx **(Rogalskyi, 2022)**.

Although the RCA is the dominant vessel in most hearts, it is important to consider that it is usually the LAD that supplies the majority of the left ventricular myocardium as well as the anterior and mid thirds of the interventricular septum **(Rogalskyi, 2022)**.

**B.3. Coronary veins**

The coronary veins return deoxygenated blood from the myocardium back to the right atrium. Most venous blood returns via the coronary sinus. Coronary venous anatomy is highly variable, but is generally comprised of three groups:

Cardiac veins which drain into the coronary sinus:

Great cardiac vein

Middle cardiac vein

Small cardiac vein

Posterior vein of the left ventricle

Vein of marshall (oblique vein of the left atrium)

The anterior cardiac veins which drain directly into the right atrium.

The venae cordisminimae (smallest cardiac veins a.k.a. Thebesian veins) drain directly into all four chambers but are most frequent in the right atrium **(Weerakkody, 2023)**.

**II. 1. C. The wall of the heart**

The wall of the heart separates into the following layers: epicardium, myocardium, and endocardium. These three layers of the heart are embryologically equivalent to the three layers of blood vessels: tunica adventitia, tunica media, and tunica intima, respectively. A double-layer, fluid-filled sac known as the pericardium surrounds the heart. The two layers of the pericardium are called the outer fibrous/parietal pericardium and the inner serous/visceral pericardium. The epicardium constitutes the visceral pericardium, underlying fibro-elastic connective tissue, and adipose tissue **(Rodriguez and Tan, 2017)**.

**Epicardium**

is a protective layer consists mostly of connective tissue and forms the innermost layer of the pericardium **(Kohli, 2020)**.

This is a thin protective coating that surrounds the other parts **(Kohli, 2020).**

The pericardium is a fibrous sac that encloses the heart and great vessels. It keeps the heart in a stable location in the mediastinum, facilitates its movements, and separates it from the lungs and other mediastinal structures. It also supports physiological cardiac function (Figure 11) (Figure 12) **(Rehman et al., 2022)**.

**Myocardium**

It is the muscular tissue of the heart (Figure 11) **(Kohli, 2020)**.

**Endocardium**

This tissue lines the inside of the heart and protects the valves and chambers (Figure 11) **(Kohli, 2020)**.

**II. 1. D. Valves**

Valves are an important component of the heart. Not only do they act as an exit gate, but they also prevent backflow into the chamber. The aortic valve, separating the aorta from the left ventricle, and the pulmonic valve, separating the pulmonary artery from the right ventricle, are known as semilunar valves. The two atrioventricular (AV) valves are the tricuspid and mitral valves. The tricuspid valve marks the separation between the right atrium and right ventricle, while the mitral valve separates the left atrium from the left ventricle. A unique aspect of the AV valves is their attachments to the ventricles with the assistance of chordae tendinae inserted onto the papillary muscle of the ventricles (Figure 13) **(Arackal and Alsayouri, 2019).**

The valves of the human heart can be grouped in two sets:

**D.1.Atrioventricular valves**

It prevent backflow of blood from the ventricles into the atria.

**D.1.1.Tricuspid Valve**

Tricuspid or right atrioventricular valve, it is between the right atrium and right ventricle.

**D.1.2.Mitral Valve**

Mitral or bicuspid valve, it is between the left atrium and left ventricle.

**D.2.Semilunar valves**

It prevent the backflow of blood into the ventricle.

**D.2.1.Pulmonary Valve**

Pulmonary or Pulmonic Valve, It is located at the opening between the right ventricle and the pulmonary trunk.

### D. 2. 2. Aortic valve

It is located at the opening between the left ventricle and the aorta (Figure 13) **(Curtis, 1992).**

## II. 2. Histological section of the myocardium

The myocardium is composed of individual striated muscle cells (fibers), 10 to 15 µm in diameter and 30 to 6o µm in length. Under the light microscope each fiber contains multiple cross-banded strands (myofibrils), which run the length of the fiber and are composed of a serially repeating structure, the sarcomere. The remainder of the cytoplasm, lying between the myofibrils, contains other cell constituents such as the single centrally located nucleus, numerous mitochondria, and intracellular membrane systems (Figure 14) **(Braunwald, 1971)**.

## II. 3. Cardiac cycle

Cardiac cycle is the expression referring to the events related to the flow and blood pressure that occur from the beginning of a heart beat until the next beat.

Like a pump, the heart works in two phases: systole and diastole. At systole the right ventricle contracts to eject the venous blood into the lungs so that they are oxygenated, and in the left ventricle contraction ejects oxygenated blood into the entire systemic circulation. This occurs with the closure of the atrioventricular valves (mitral and tricuspid) and opening of the pulmonary and aortic valves. The right ventricle contracts, increases the pressure inside that opens the pulmonary valve leading the blood from the right ventricle to the pulmonary artery. Contralaterally, the left ventricle contracts, increasing pressure by opening the aortic valve leading the blood from the left ventricle into the circulation. In the diastole the relaxation and decrease of pressure in the ventricles occurs, so that the tricuspid and mitral valves open and fill the ventricles with the blood coming from the atrial **(Barros, 2019)**.

Heart failure is defined as the pathologic state in which the heart is unable to pump blood at a rate required by the metabolizing tissues or can do so only with an elevated filling pressure. Heart failure in adults most frequently results from the inability of the left ventricle to fill (diastolic performance) or eject (systolic performance) blood. The severity of heart failure and its prognosis are more closely related to the degree of diastolic filling abnormalities than the ejection fraction, which underscores the importance of understanding the mechanisms of diastolic abnormalities in heart failure **(Fukuta and Little, 2008)**.

Diastolic heart failure (DHF) and systolic heart failure (SHF) are 2 clinical subsets of the syndrome of chronic heart failure that are most commonly encountered in clinical practice.

Diastole is defined as “the dilatation of the heart with blood: opposed to systole, or contraction.” Conventionally, the closure of the aortic valve is regarded to indicate the onset of diastole as it indicates the onset of ventricular relaxation phase. Because left ventricular ejection influences relaxation and the rapid filling, it has been suggested that these phases should be considered phases of systole. The most commonly accepted view, however, is that the… **(Chatterjee and Massie, 2007)**.

## II. 4. Function of the heart

Managing blood supply, the variations in the rate and force of heart contraction match blood flow to the changing metabolic needs of the tissues during rest, exercise, and changes in body position.

Producing blood pressure, the contractions of the heart produce blood pressure, which is needed for blood flow through the blood vessels.

Securing one-way blood flow, the valves of the heart secure a one-way blood flow through the heart and blood vessels.

Transmitting blood, the heart separates the pulmonary and systemic circulations, which ensures the flow of oxygenated blood to tissues **(Belleza, 2023)**.

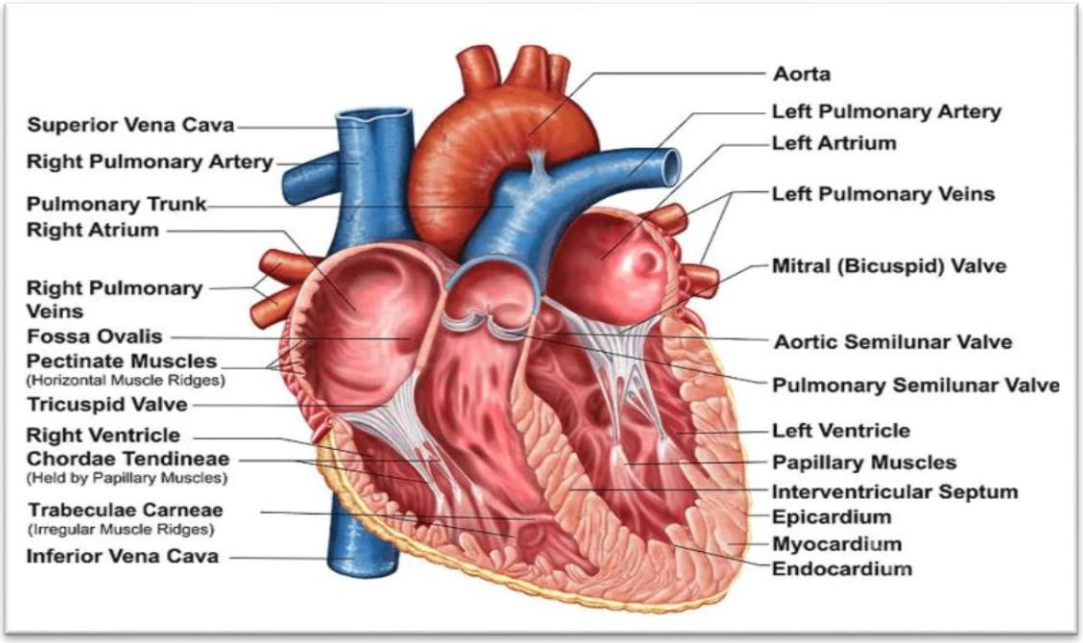



**Figure 10:** structure of the heart (Site web 7).

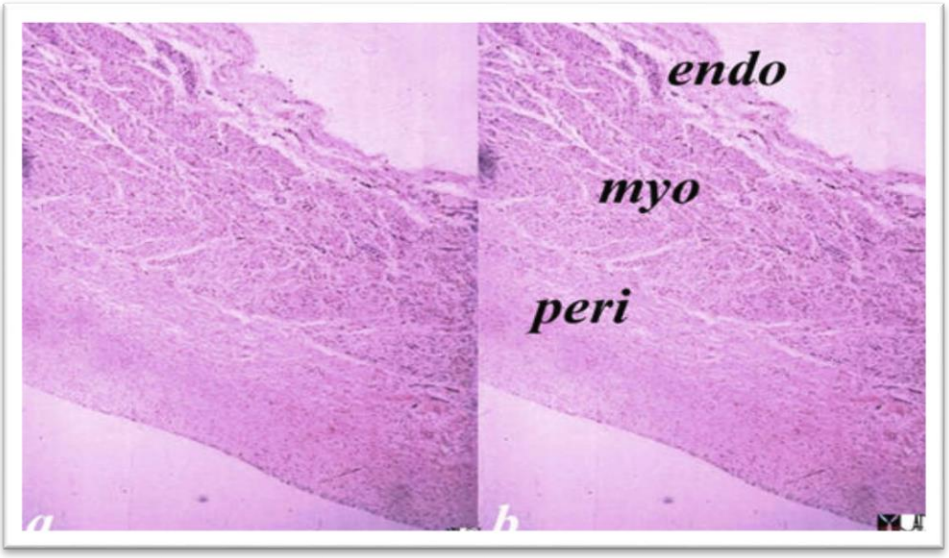



**Figure 11:** histological section shows the inner layer called the endocardium (endo) which lines the inner portion of the cavity and the myocardium (myo) is the middle layer which in this case is relatively thin since it is from the atrium, and then the outer pericardium (peri) (Site web 08).

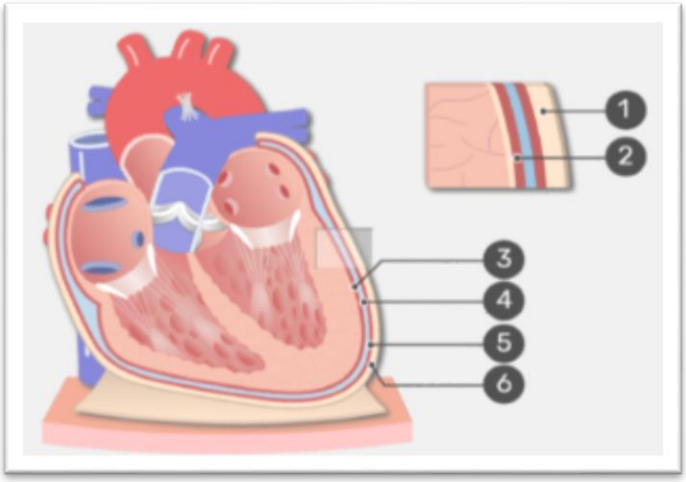



**Figure 12:** structure and function of pericardium. 1: outer wall. 2: inner wall. 3: visxeral pericadium. 4: pericardial cavity. 5: fibrous pericardium. 6: fibrous pericardium (Site web 9).

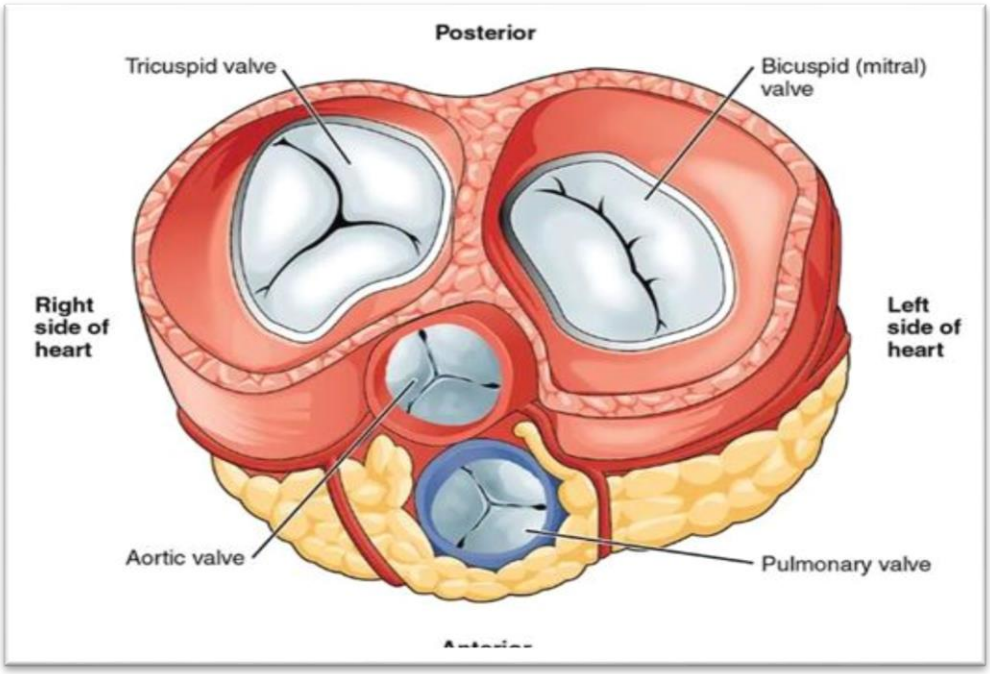



**Figure 13:** four heart valves **(Belleza, 2023)**.

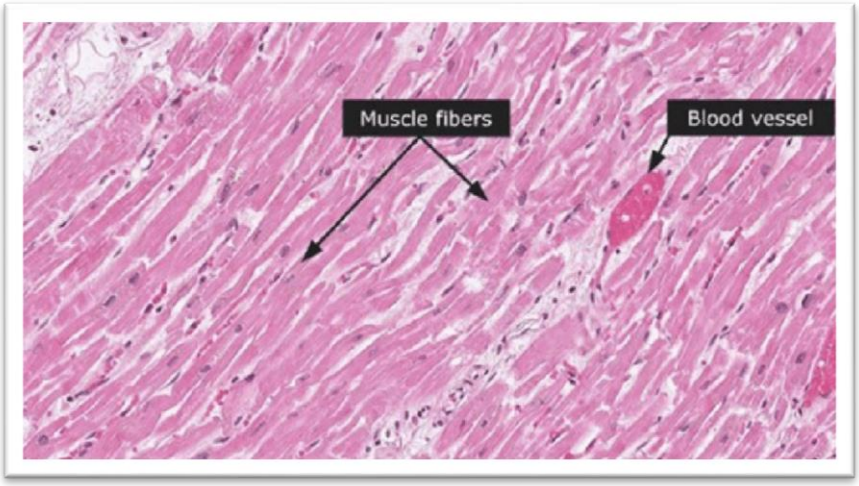



**Figure 14:** histologic section of a normal myocardium of a control case. Arrows shows normal muscle fiber and blood vessel. Heamatoxylin and eosin stain, 40× original magnification. (Site web 10)**.**

## II. 5. Atherosclerosis

### II. 5. 1. Definition

The term atherosclerosis is 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-Kopaei et al., 2014)**.

Atherosclerosis is a chronic, inflammatory disease of the arterial wall that underlies many of the common causes of cardiovascular morbidity and mortality, including myocardial infarction (MI), and cerebrovascular and peripheral vascular disease. Early pathological descriptions viewed atherosclerosis 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 15) **(Douglas and Channon, 2014)**.

The lesions result from an excessive, inflammatory-fibroproliferative 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)**.

### II. 5. 2. Causes of atherosclerosis

Development of atherosclerotic lesions probably requires low-density lipoprotein, a particle that carries cholesterol through the blood (Figure 16). 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 Visseren, 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).**

### II. 5. 3. Stages of atherosclerotic plaque

Atherosclerosis has several stages of information and progression of plaque which are briefly described in the following (Figure 17):

#### II. 5. 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 then oxidize 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 develops 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)**.

#### II. 5. 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 atheroma. Proteoglycans that are secreted from extracellular 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 **(Reddy, 2020)**.

#### II. 5. 3. 3- Thin-cap fibroatheroma 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 thrombogenesis which is a life-threatening risk. This occurs mainly in the cardiovascular system leading to many diseases. The ruptured caps sometimes heal and involve again the accumulation of collage leading progression of atheromatous plaque **(Reddy, 2020)**.

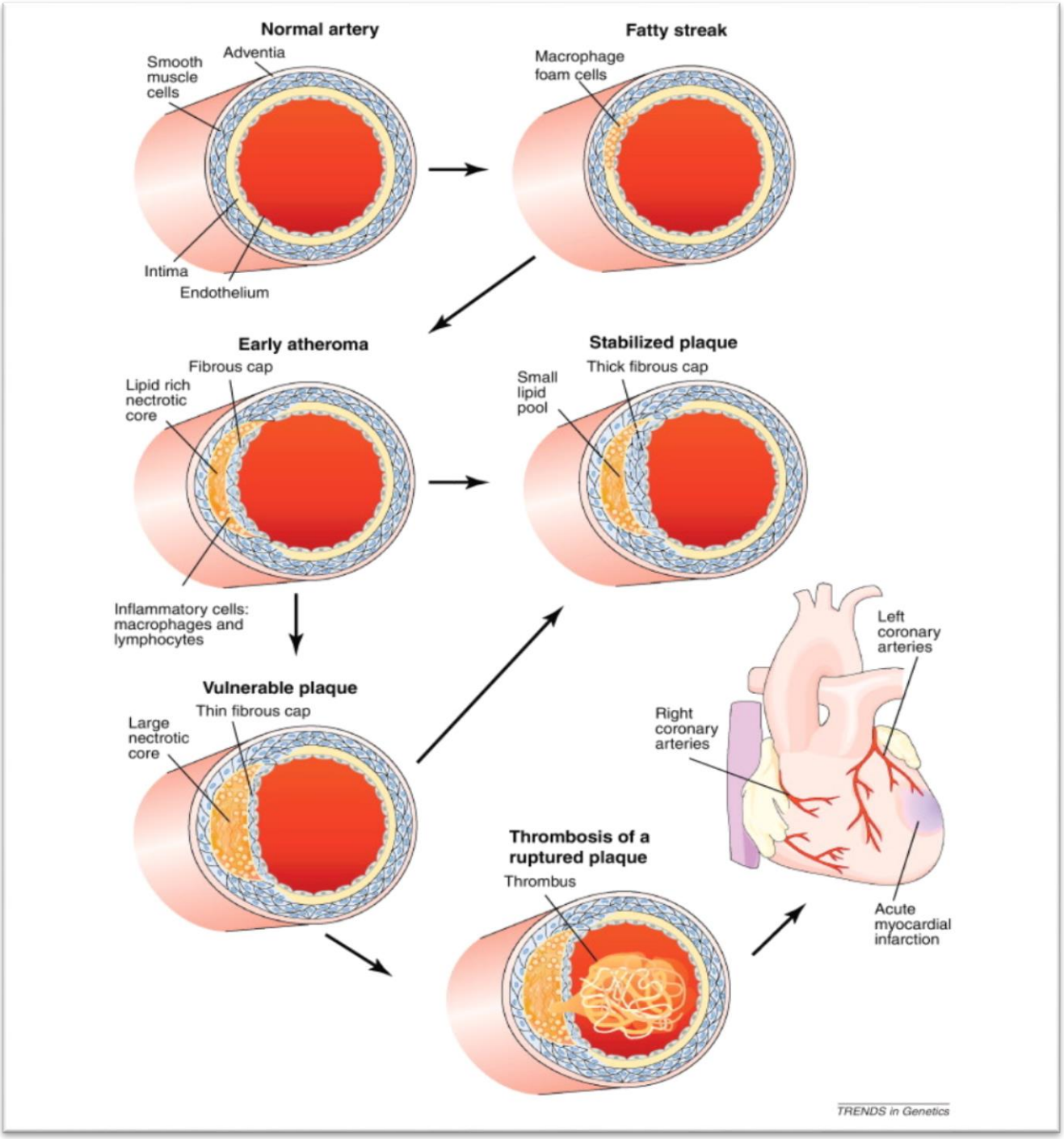



**Figure 15:** different stages in progression of atherosclerosis

(Site web 11).

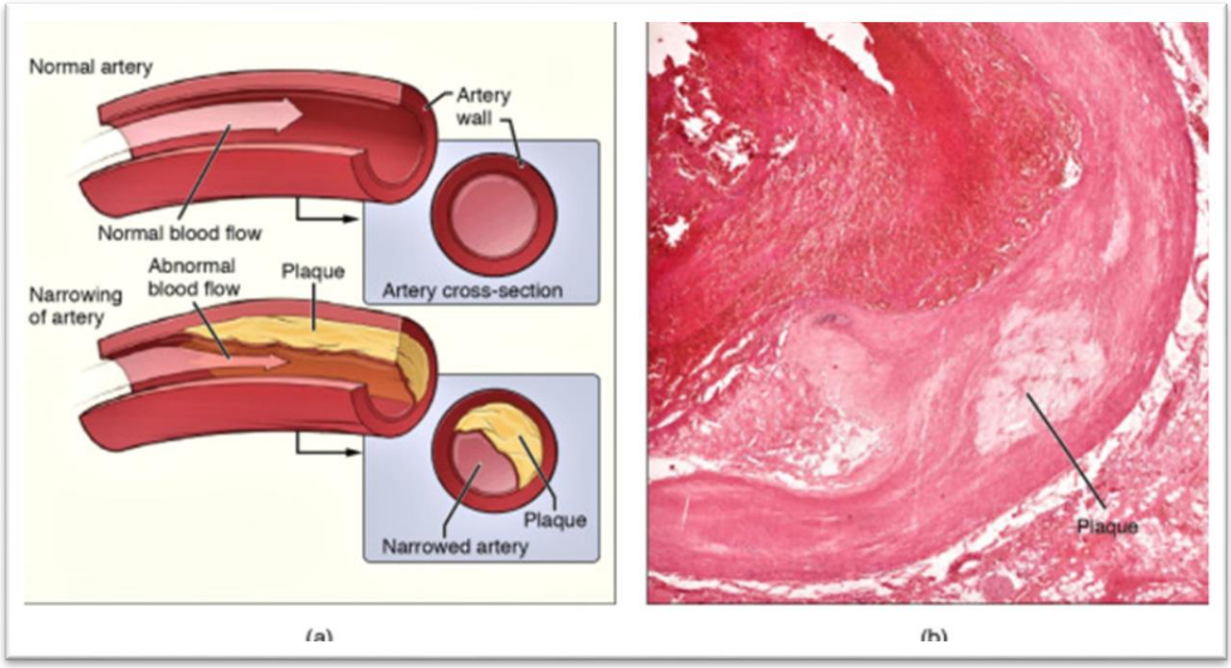



**Figure 16:** atherosclerosis (Site web 12).

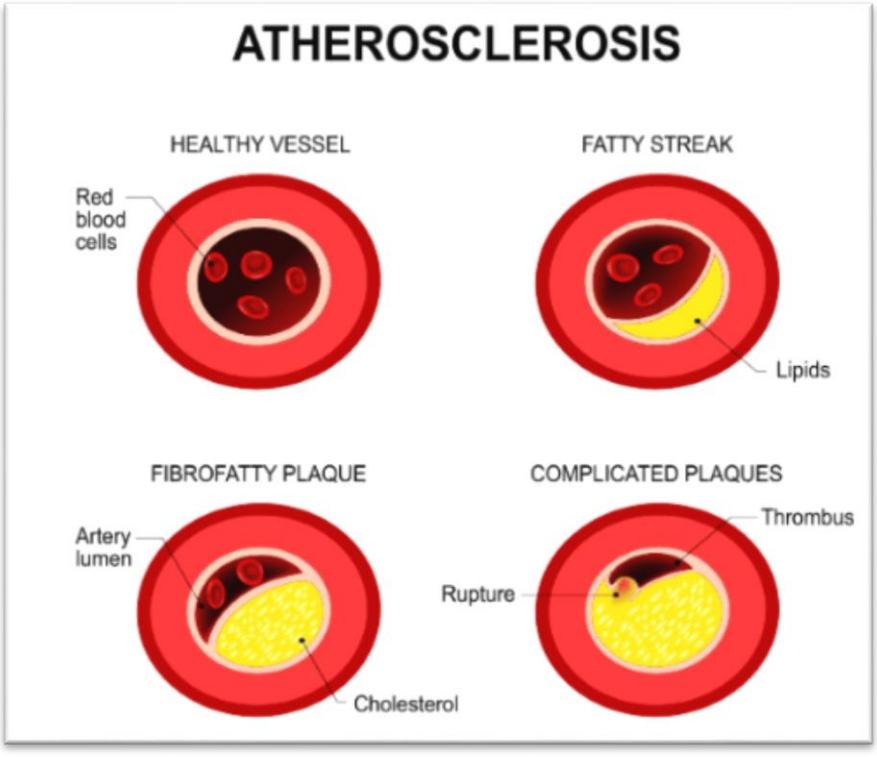



**Figure 17:** stages of atherosclerosis. Detailed illustration. Healthy artery and unhealthy arteries. Transverse section of the humans artery (Site web 13).

## II. 6. 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 cardiovascular 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, increased platelet reactivity, hypercoagulability, lipoprotein (a), 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. In this review, we discuss the evidence associating these factors in the pathogenesis of atherosclerosis, the mechanism of risk, and the clinical implications of this knowledge **(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)**.

### Endothelial dysfunction

Normal endothelium functions in an inhibitory mode; it inhibits smooth muscle contraction, platelet aggregation, vascular smooth muscle growth, thrombobosis, 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)**.

### Hypertension

Hypertension is an independent indicator of increased risk of coronary events. Reduced EDRF 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)**.

**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 effect is not likely to result solely from the favorable lipid alterations associated with hot mone replacement **(Glasser et al., 1996).**

**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. His conclusions suggest that elevated glucose can cause characteristic dysfunctions of the endothelium in the regulation of vascular tone **(Glasser et al., 1996)**.

# Chapter III: hot water and traditional yeast

# Hot water and traditional yeast

## III. I. Hot water

### III. I. 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 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 **(Raschke, 2006)**.

### III. I. 2. Structure

Water molecules are V-shaped with molecular formula H2O **(Xiao, 2014)**. 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 18) **(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 19) **(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 interactionswith itself, other molecules and ions **(Sharp, 2001)**.

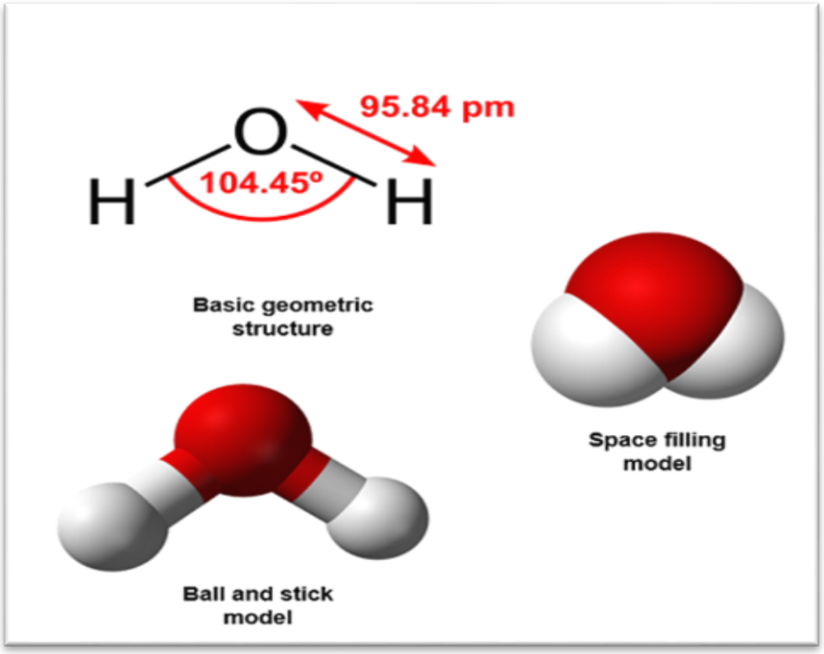



**Figure 18:** water molecules (Site web 14).

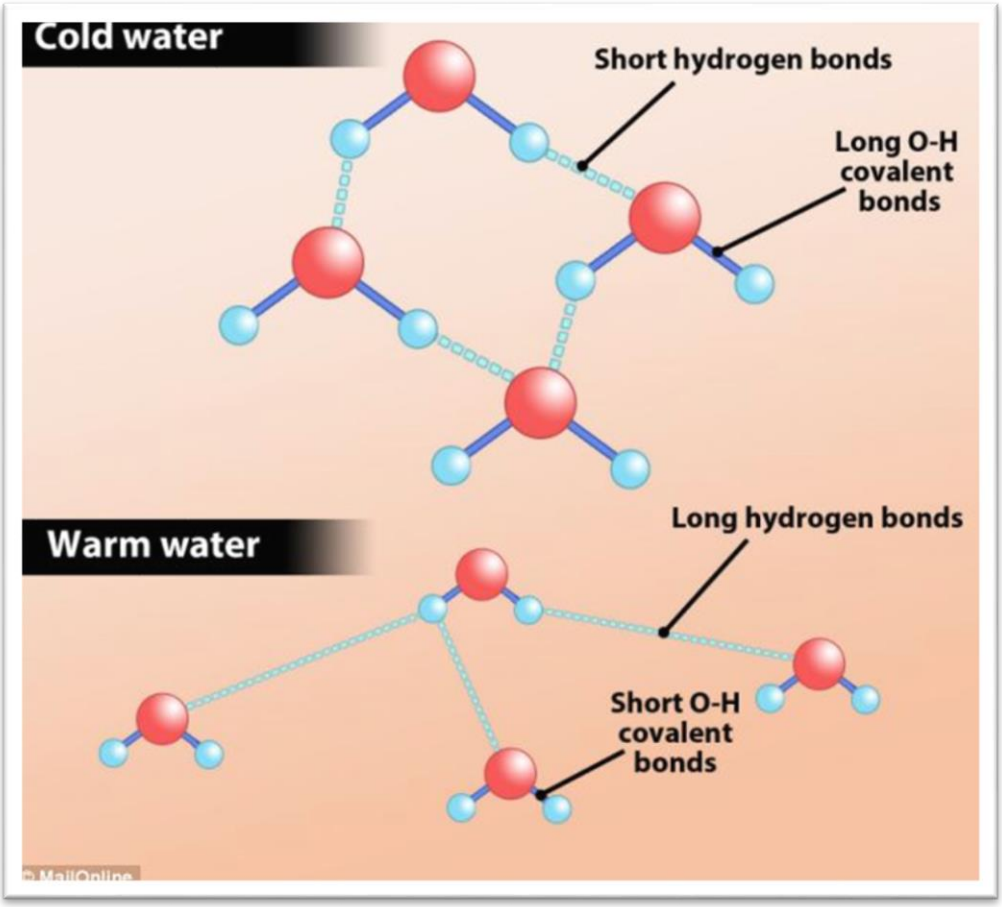



**Figure 19:** cold and warm water structure (Site web 15).

## III. I. 3. Hydrotherapy

### III. I. 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: neutrotherapy, thermotherapy and cryotherapy 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 03:** techniques and uses of hydrotherapy **(Chowdhury et al., 2021)**.

| | |
|---|---|
| **Techniques of hydrotherapy** | Kneipp system, 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. |

### III. I. 4. Benefits of drinking hot water

Drinking hot water leads to healthier digestion and consuming it daily leads to help in body detoxification 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)**.

## III. II. Traditional yeasts

### III. II. 1. Definition

Sourdough" is one of the oldest forms of cereal fermentation utilized primarily for baking purposes and it has been proven to be perfect for upgrading the shelf life, texture, palatability, and nutritional values of wheat and rye breads. Its main function is to leaven the dough to produce more aerated bread **(Behera and Ray, 2015)**.

It is dough that tastes sour due to the high levels of acids produced intentionally or unintentionally by microorganisms or by the addition of acid. The bread produced from such dough is called sour bread **(Amr and Alkhamaiseh, 2022)**.

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-path et al., 2022)**.

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

**Yeasts species**

The most widespread yeast species in sourdough are "*Saccharomyces cerevisiae*, *Kazachstaniahumilis* (previously named *Candida humilis*), *Kazachstaniaexigua*, *Pichiakudriavzevii*, and *Torulasporadelbrueckii*" **(Carbonetto et al., 2020)**.

## III. II. 2. 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 (Figuge20) **(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)**.

## III. II. 3. Formulation yeasts

*Sourdough starter* can be considered as a mixture of water and flour fermented by yeasts and bacteria (Figur 22) **(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 21) **(De et al., 2021)**.

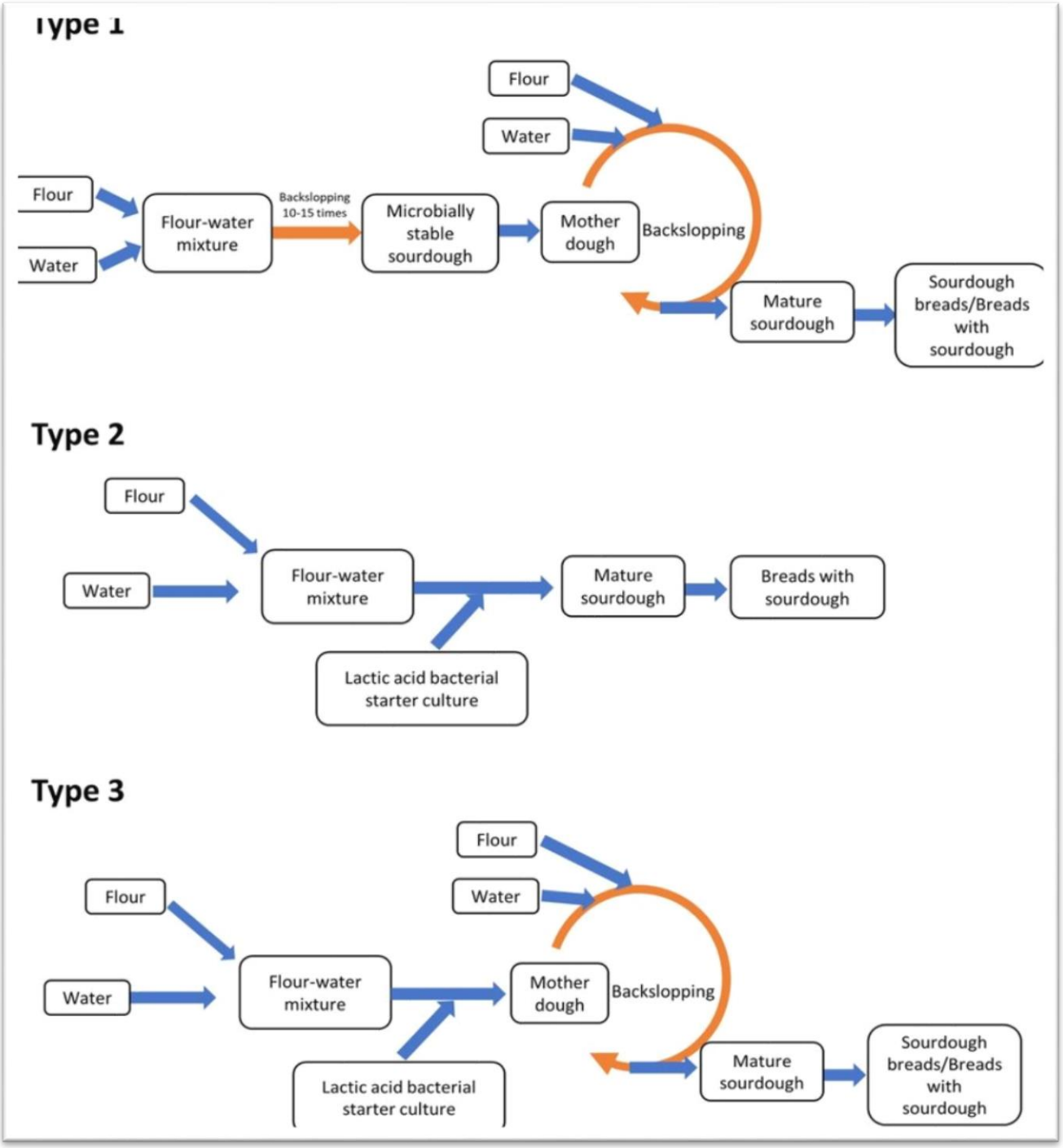



**Figure 20:** types of sourdough starter: various types of sourdough production processes based on the way of inoculation of the flour-water mixture **(De et al., 2021)**.

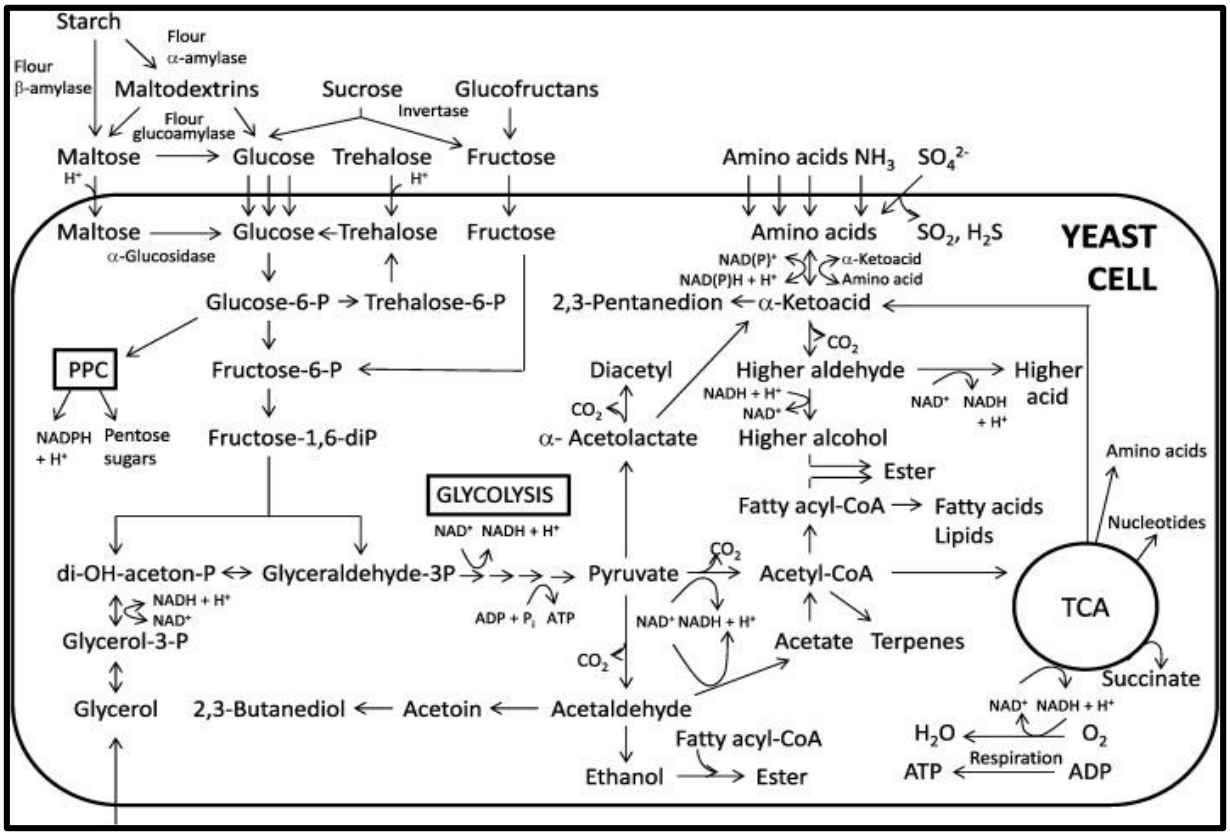



**Figure 21:** overview of the metabolism of yeasts in a sourdough matrix **(De et al., 2021)**.

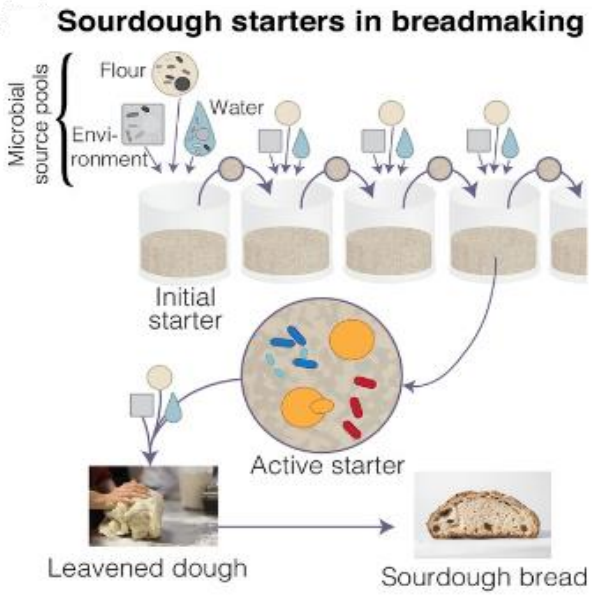



**Figure 22:** sourdough starters in breadmaking **(Landis et al., 2021)**.

## III. II. 4. 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, 2022)**.

**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, 2022)**.

**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 lose weight **(Blackwood, 2022)**.

**Good for nerve function:** dry yeast has thiamine, riboflavin, vitamin B6 and folate, which promote nerve health **(Marengo, 2023)**.

**Promotes healthy aging:** 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. A 2019 review in the journal Nutrients found that fermented grain-based products, like sourdough, have antioxidant, anti-hypertensive, anti-diabetic and FODMAP-reducing qualities **(Ball, 2022)**.

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)**.

# Material and methods

# VI. Material and methodes

## VI. 1. Material

### VI. 1. 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 (60%, 70%, 95% and 96%), HCl, NaOH, NaCl, butanol, xylene, paraffin and glycerin, acetic acid, heamatoxylin eosin, NaH2PO4, Na2HPO4, Coomassie Brilliant Blue G-250.

### VI. 1. 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 (Figure 23).

**Figure 23:** materials used during experimental work.

### Choice of treatment

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

### Animals

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

## VI. 2. Methods

### VI. 2. 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 standad diet and drunk hot water at fifty degrees.

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

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

**Group sugar + yeast (S+TY, G6):** group was fed on standard diet rich in sugar with traditional yeast and drinking water at room temperature (Table 04). The diet and weight were measured every day at the same time during 21days of treatment.

**Table 04:** treatment of mice for 21 day.

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

### VI. 2. 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 heart 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).

### VI. 2. 3. Biochemical investigation

#### 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, ASAT and 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 -20°C until the determination of proteins and reduced glutathione concentrations.

### 2- Glutathione reduced measurment

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 (Figure 32).

## 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 (Figure 24) (Tabel 07).

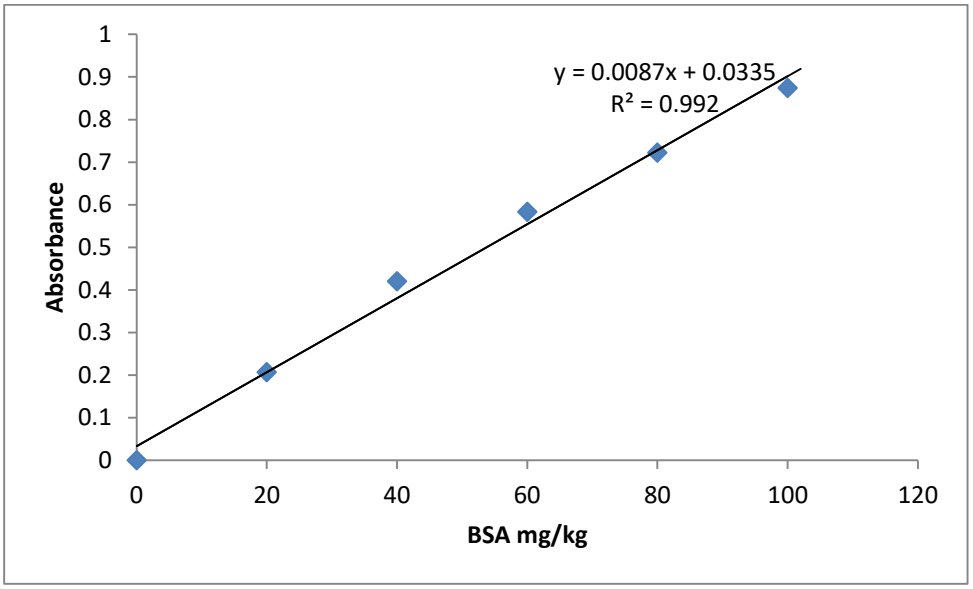



**Figure 24:** calibration graph of bovine serum albumin

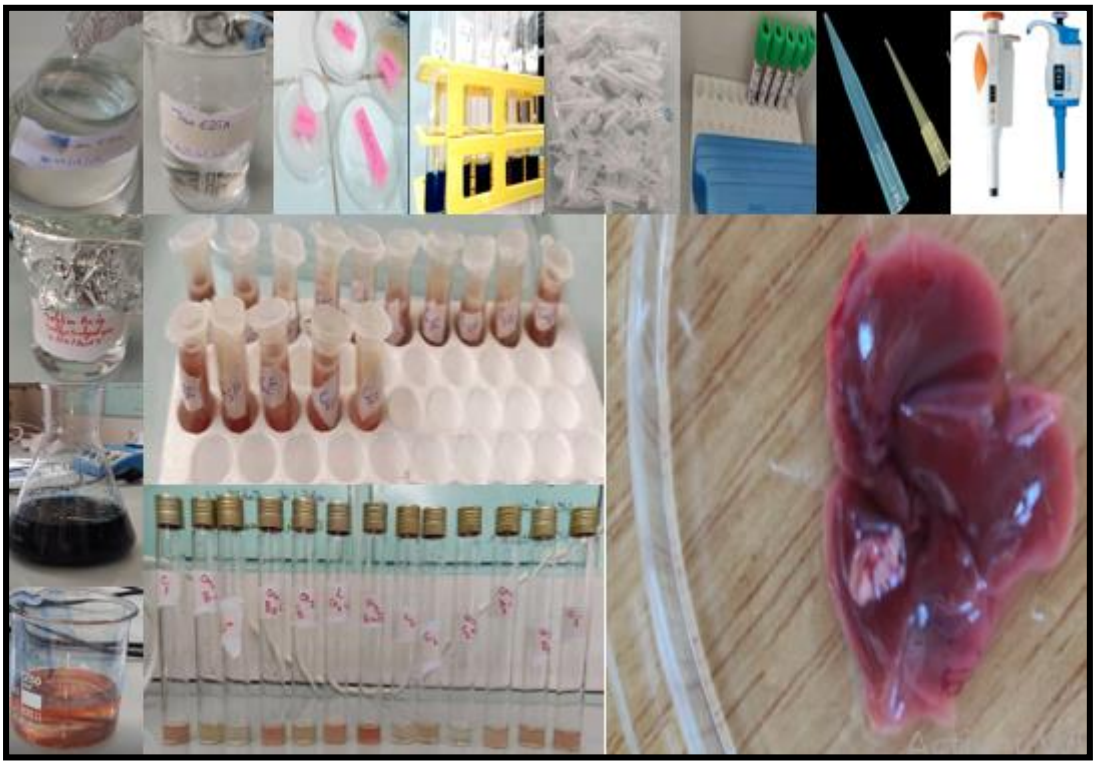


**Figure 25:** materials and solutions used in protein determination and glutathione.

## VI. 2. 4. Preparation of histological sections

### Fixation

The heart was fixed in the formol 10% solution as shown before.

### 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.

### Insertion into paraffin

In the next step, the organs were 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.

**Coloring stage**

The samples were placed in two xylene baths for 10 minutes each.

Samples 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 the samples were washed with tape water.

The samples immersed in ethanol (96%) for 1 minute, then placed in two xylene baths for 2 minutes each.

Samples are dried in the oven at a temperature of 38 degrees. After this stage, the samples are ready for viewing under a microscope.

## VI. 2.5 Statistical analysis

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

# Results and discussion

# V. Result and discussion

## V. 1. Results

### V. 1. 1. Weight and food consumed

#### 1.1. First experience (Group C)

The objective of this experiment is to evaluate the effect of normal food on the weight of mice and the consumption of food.

##### 1.1.1. Change in 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 (Figure 26).

##### 1.1.2. Food consumption

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 (Figure 27).

#### 1.2. Second experience (Group S)

The objective of this experiment is to evaluate the effect of food rich in crystallized sugar on mice.

##### 1.2.1. Change in weight

Our results demonstrated that in the group administrated with crystallize sugar in the first and the third week was (35.81g±0.41) (36.07g±1.44) respectively (Figure 26).

##### 1.2.2. Food consumption

Our results demonstrated that in the group administered with crystallize sugar, the food consumption in the first week was (42.57±28.05) and third week was (99.57g±18.54), the food consumed by mice is increased respectively (Figure 27).

#### 1.3. Third experience (Group Hw)

The objective of this experiment is to evaluate the effect of hot water in mice fed a normal food.

##### 1.3.1. Change in weight

Our results demonstrated that in the group of mice treated with hot water in the first week the weight was (33.01g±0.71) and in the third week was (33.17g±0.74) (Figure 26).

### 1.3.2. Food consumption

Our results demonstrated that in the group of mice treated with hot water, in the first week the Food consumption was (63.57g±18.97) and in the third week was (82.71g±29.09) (Figure 27).

## 1.4. Fourth experience (Group TY)

The objective of this experiment is to evaluate the effect of traditional yeast in mice

### 1.4.1. Change in weight

Our results demonstrated that in the group administered with traditional yeast, in the first week the weight was (30.50g±1.74) and in the third week was (33.13g±2.32) (Figure 26).

### 1.4.2. Food consumption

Our results demonstrated that in the group administered with traditional yeast, in the first week the food consumption was (84.14±19.11) and in the third week was (76.41±42.05) (Figure 27).

## 1.5. Fifth experience (Group S+Hw)

The objective of this experiment is to evaluate the effect of hot water in mice fed a high-crystallized sugar diet.

### 1.5.1. Change in weight

Our results demonstrated that the weight is increased in the group administered with crystallized sugar and treated with hot water, in the first week was (33.60g±0.99) and in the third week was (34.11g±3.01) (Figure 26).

### 1.5.2. Food consumption

Our results demonstrated that the food consumed by mice is increased in group administered with crystallized sugar and treated with hot water, in the first week was (80.14g±183.30) and in the third week was (92.42g±28.98) (Figure 27).

## 1.6. Sixth experience (Group S+TY)

The objective of this experiment is to evaluate the effect of traditional yeast in mice fed a high-crystallized sugar diet.

### 1.6.1. Change in weight

Our results demonstrated that the weight is increased in the group administered with crystallized sugar and treated with traditional yeast, in the first week was (29.27g±2.25) and in the third week was (31.60g±1.89) (Figure 26).

### 1.6.2. Food consumption

Our results demonstrated that the food consumed is decreased in group administered with crystallized sugar and treated with traditional yeast, in the first week was (68.71±29.43) and in the third week was (42.83±41.03) (Figure 27).

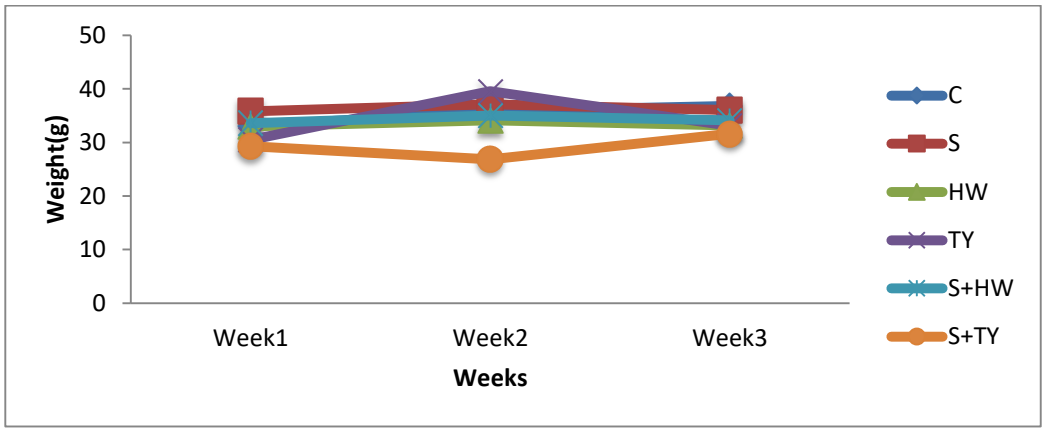



**Figure 26**: effect of crystallize sugar and hot water and traditional yeast on the weight in mice during 21 days.

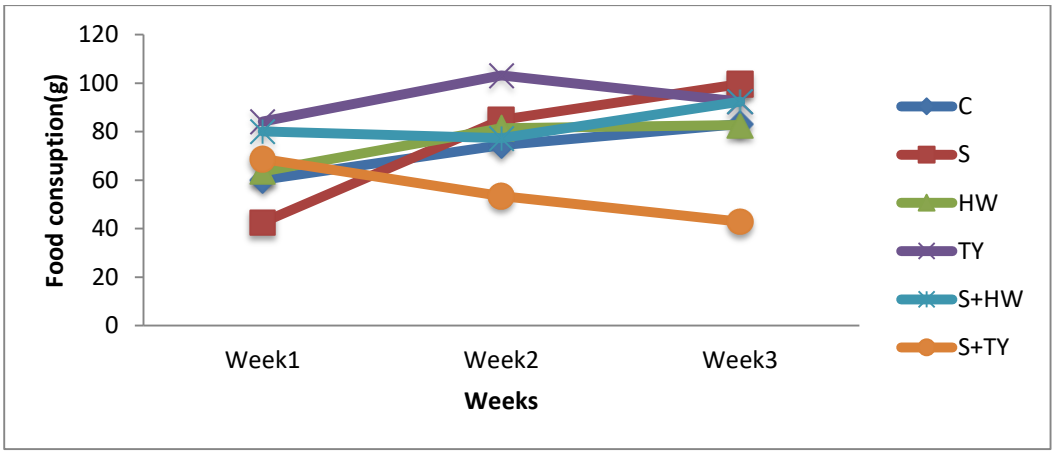



**Figure 27**: effect of crystallize sugar and hot water and traditional yeast on the food consumed by mice during 21 days.

### V. 1. 2. Biochimical analysis

**Blood sugar**

The (Figure28) 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), S+Hw (0.54g/l±0.19), TY (1.81g/l±0.10), S+TY (1.66g/l±0 .37) P<0.0001.

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

The concentration of sugar in group of animal treated with hot water is decreased but not significantly when it is compared to the group of (S) P> 0.05.

**Lipids status**

**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 group administered with crystallized sugar, (S) (1.44g/l±0.20) and (S+HW) (1.68g/l±0.20) and the group administered with traditional yeast, (TY) (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 the group (TY+S)(1.03g/l±0.28) when compared to the control group P>0.05 (Figure 29).

**Triglyceride**

The data showed a difference very higly 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) (Figure 30) 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

**HDL-c**

The data showed a difference in the values of HDL-C in groups (S) were (1.15g/l±0.16) and (S+HW) (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) but not significantly P>0.05 (Figure 31).

**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 (S+HW) (0.16g/l±0.04) and (S+TY) (0.11g/l±0.09)but not significantly P>0.05(Figure 32).

**CRP**

The figure37 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), (SHW) (0.41mg/l±0.34) and (HW) (0.12mg/l±0.05), (TY) (0.08mg/l±0.06) and (S+TY) (0.12mg/l±0.08) when compared to the (C) (0.74mg/l±0.21) (Figure 33).

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 (S+HW) and (S+TY) significantly and highly significantly when compared to the control group P<0.05 and P<0.01 repectively.

**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) (1.74g/l±0.59) and group treated with traditional yeast (TY) (1.60g/l±0.54) but not significantly P>0.05 (Figure 34).

**Glutathione reduced**

The concentration of glutathione reduced is decreased in groups (HW) (0.016nmol /mg protein), (TY) (0.01 nmol /mg protein), (HW+S) (0.013 nmol /mg protein) and (S+TY) (0.0045 nmol /mg protein). When compared to the (C) and (S) (0.17nmol /mg protein) (0.16 nmol /mg protein) respectively (Figure 35).

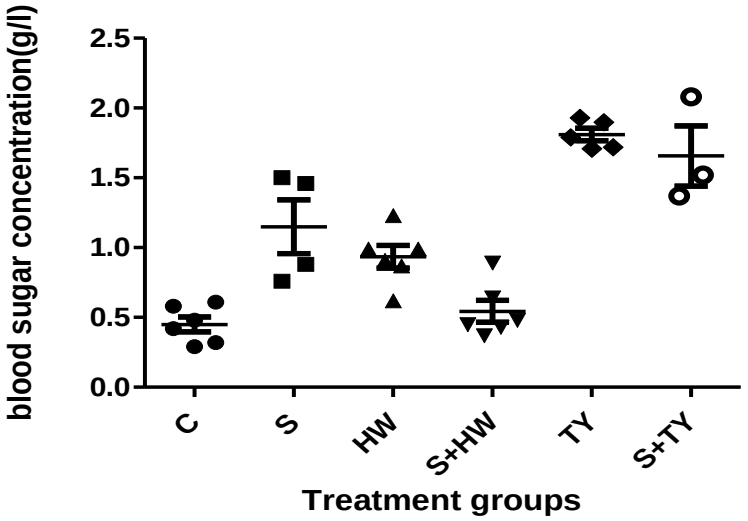



**Figure 28:** effect of high consumption of crystallize sugar, hot water and traditional yeast on fasting blood sugar in mice.

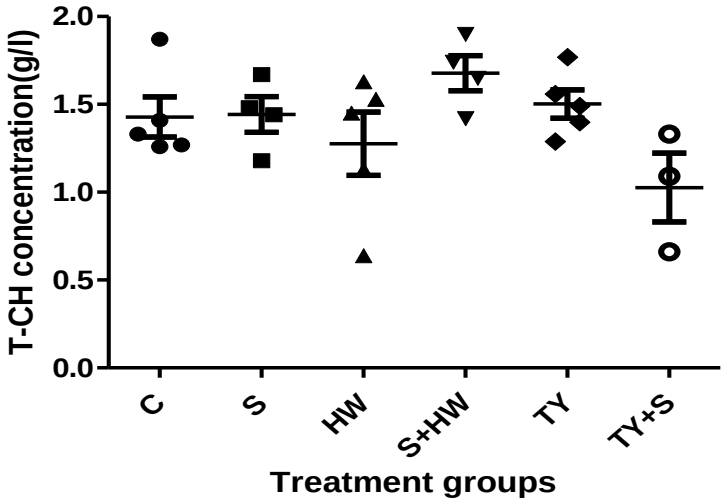



**Figure 29:** effect of high consumption of crystallize sugar, hot water and traditional yeast on T- cholesterol in mice.

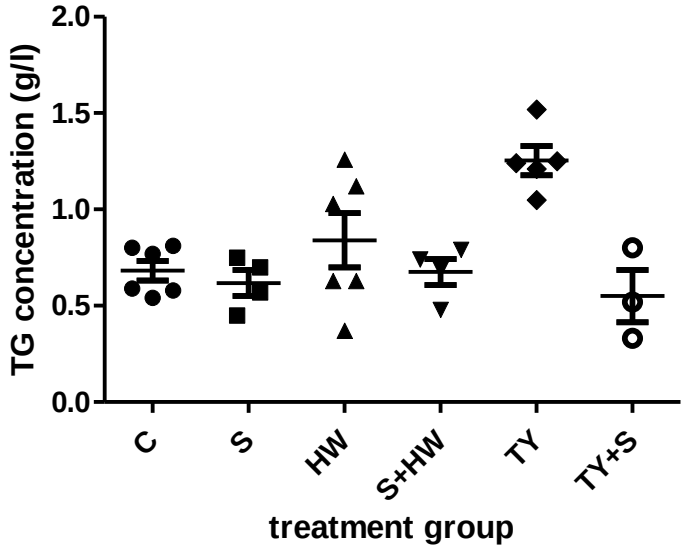



**Figure 30:** effect of high consumption of crystallize sugar, hot water and traditional yeast on triglyceride in mice.

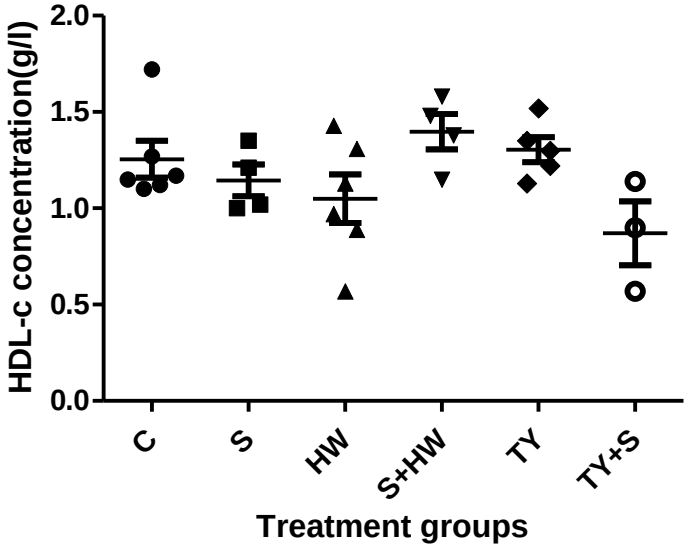



**Figure 31:** effect of high consumption of crystallize sugar, hot water and traditional yeast on HDL-C in mice.

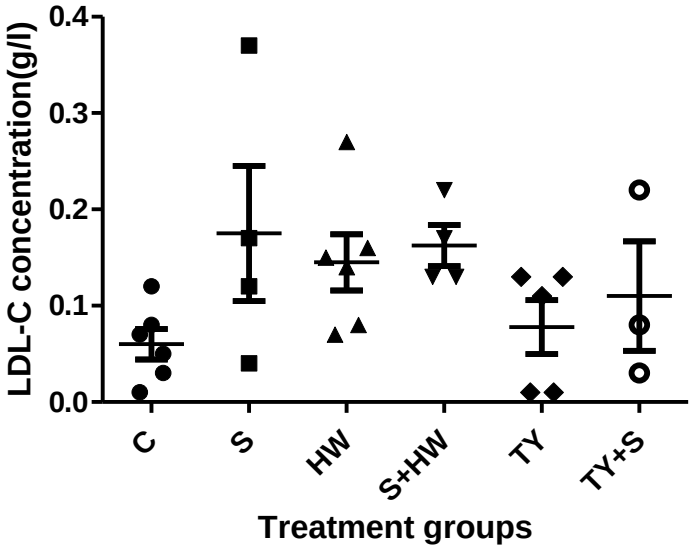



**Figure 32:** effect of high consumption of crystallize sugar, hot water and traditional yeast on LDL-C in mice.

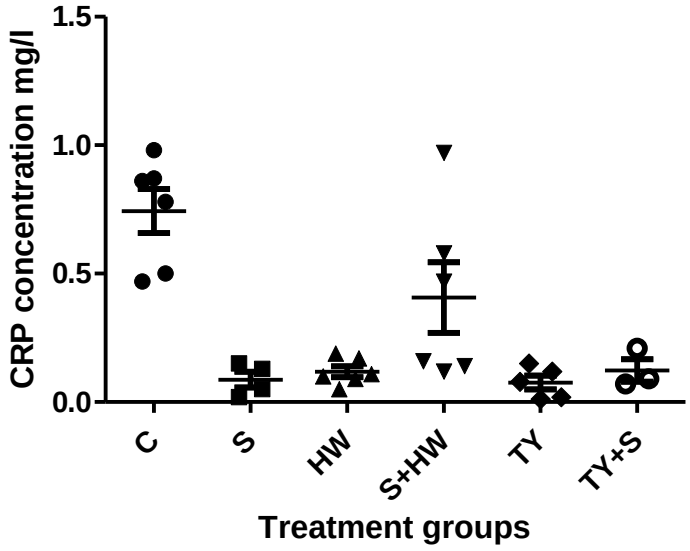



**Figure 33:** effect of high consumption of crystallize sugar, hot water and traditional yeast on CRP in mice.

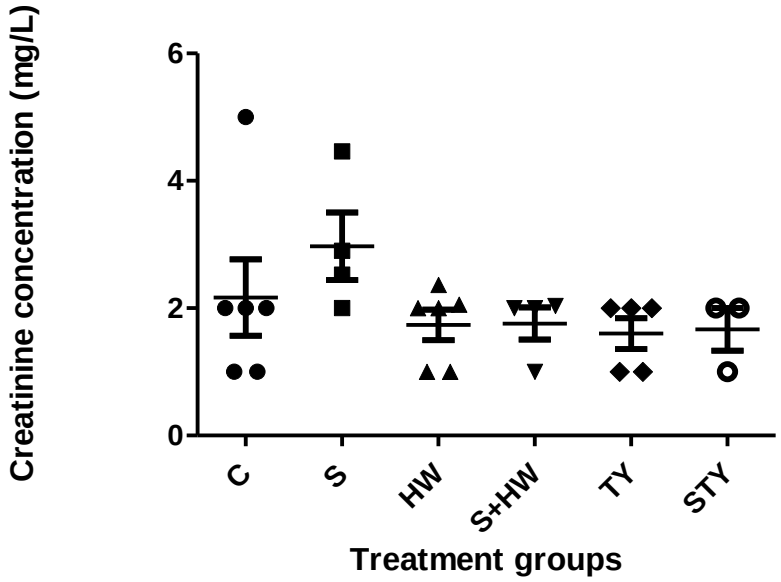



**Figure 34:** effect of high consumption of crystallize sugar, hot water and traditional yeast on creatinine in mice.

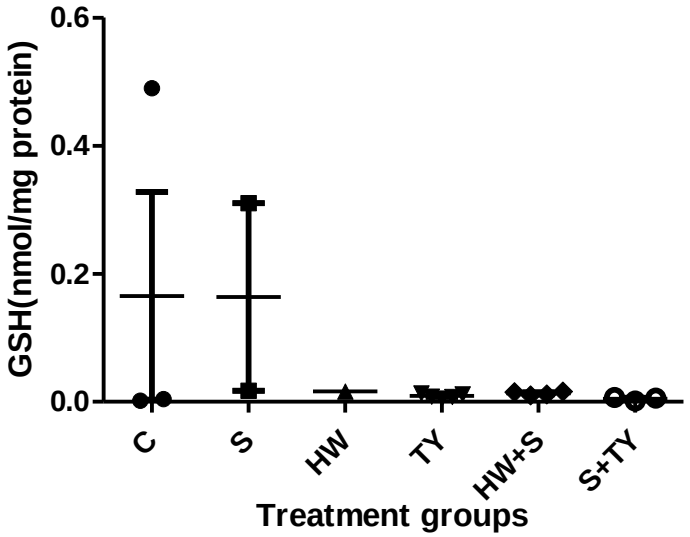



**Figure 35**: effect of high consumption of crystallize sugar, hot water and traditional yeast on GSH in mice.

**ASAT and ALAT**

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

The turkey test demonstrated that ASAT is decreased significantly in animal treated with 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) (46.55UI/L±15.25), (HW) (53.16UI/L±20.83), (S+HW) (41.10U/L±13.70), (TY) (44.07UI/L±11.29), (TY+S) (129.18UI/L±11.67) but not significantly $P>0.05$ (Figure 36, 37).

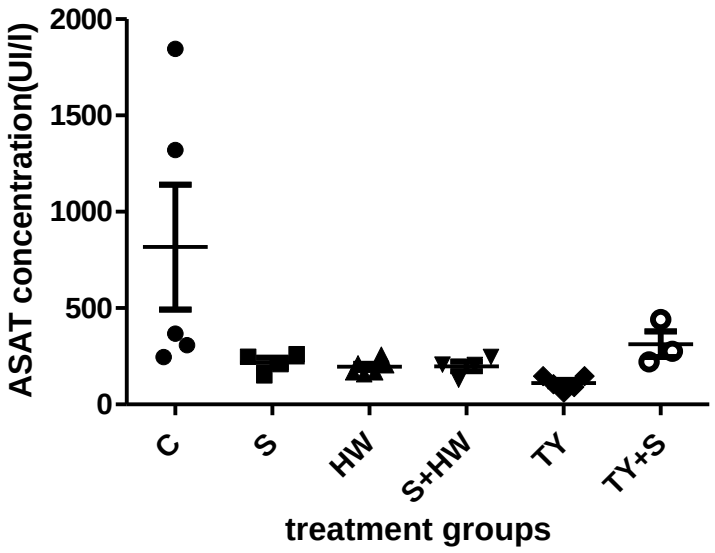



**Figure 36:** effect of high consumption of crystallize sugar, hot water and traditional yeast on ASAT in mice.

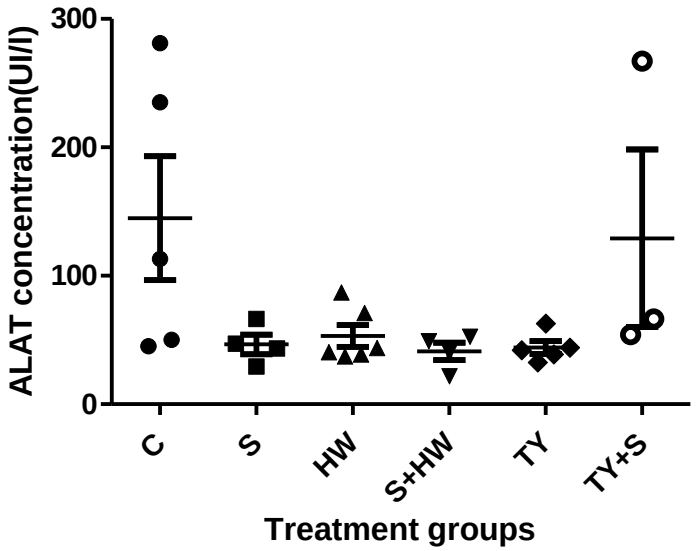



**Figure 37:** effect of high consumption of crystallize sugar, hot water and traditional yeast on ALAT in mice.

### V. 1. 3. Histological study

Microscopic observation of the heart reveals the following results:

In the group control (c), the structure of the muscle fibers of the heart and tissue are intact (Figure 38).

On the other hand, in group S there is lysis in the structure of the muscle fibers of the heart and tissue disorganization (Figure 39, 40) (Figure 40).

In groups (HW) and (TY) no pattern of lysis was observed in the structure of muscle fibers of the heart (Figure 41) (Figure 42) respectively.

For the group (S+HW), the structure of the muscle fibers of the heart isnot completely intact (Figure 43).

On the other hand, in group (TY+S) there isa lysis in the structure of the muscle fibers of the heart and tissue disorganization (Figure 44).

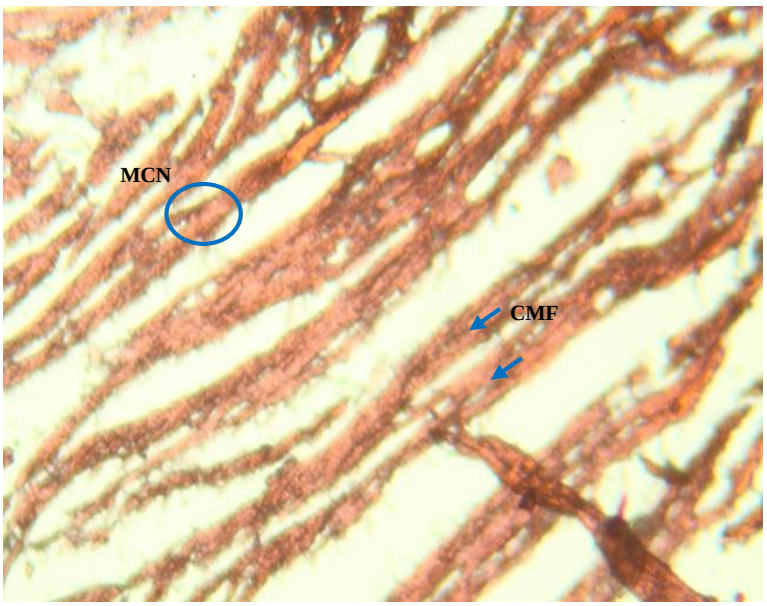



**Figure 38:** histological section of the heart control, for 21 days.

Heamatoxylin - eosine staining (G×100).

MCN: muscle cell nuclei. CMF: cardiac muscle fibers.

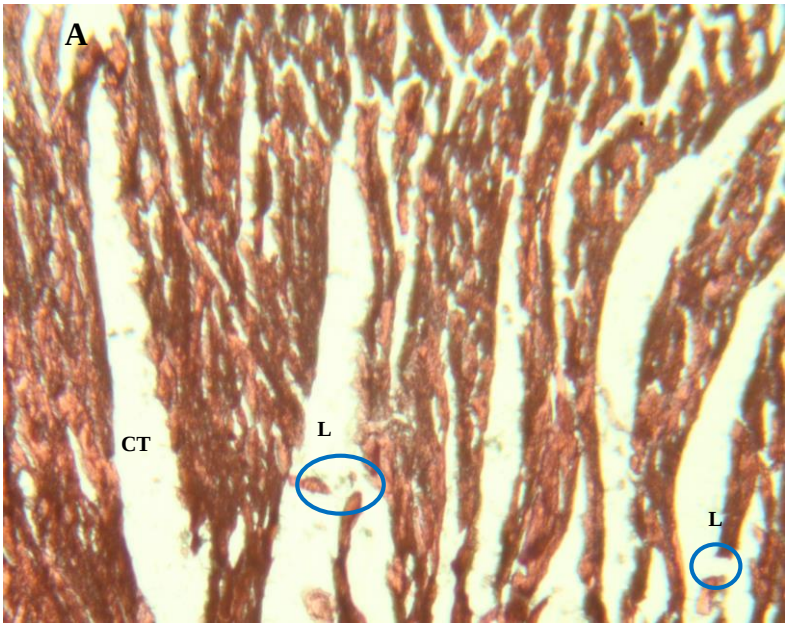



**Figure 39:** histological section of the heart treated with refined crystallized sugar for 21 days, Heamatoxylin-eosin staining (G×100).

CT: connective tissu. L: lysis.

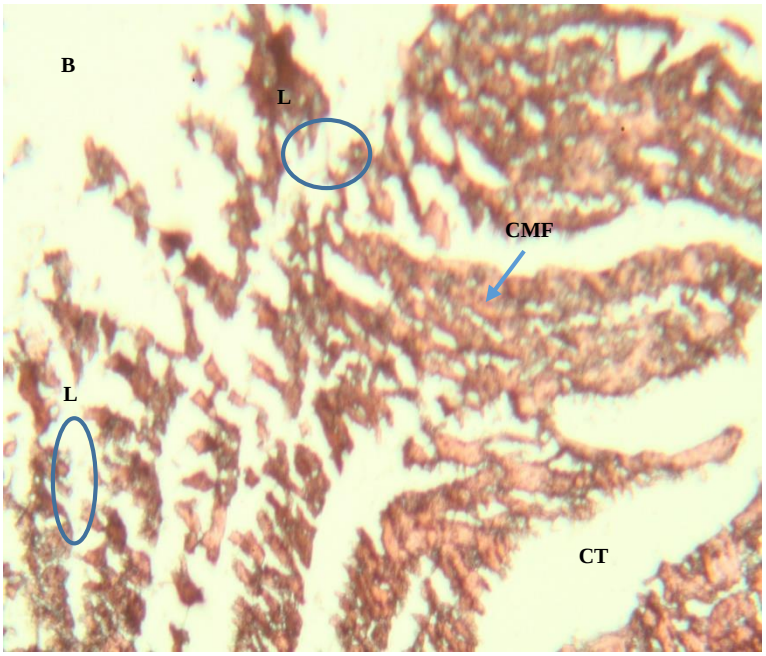



**Figure 40:** histological section of the heart treated with refined crystallized sugar for 21 days Heamatoxylin-eosin staining (G×100).

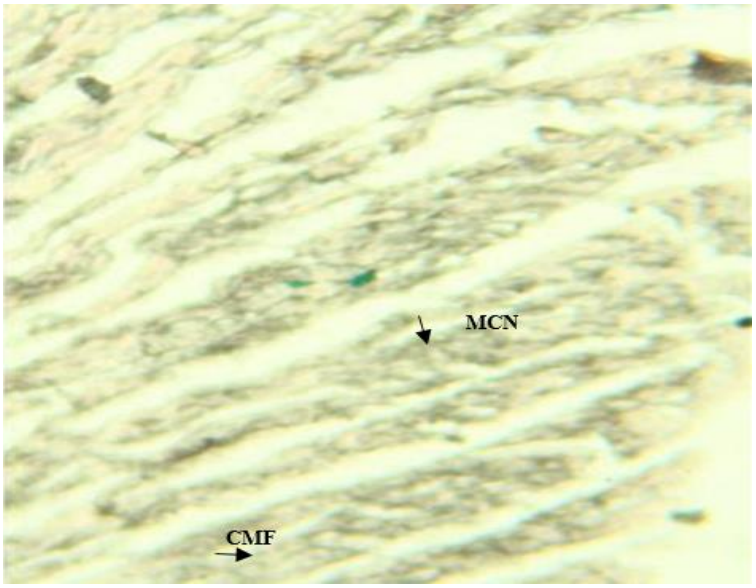



**Figure 41:** histological section of the heart treated with hot water during 21 days, Heamatoxylin-eosin staining (G×100).

MCN: muscle cell nucleus. CMF: cardiac muscle fibers.

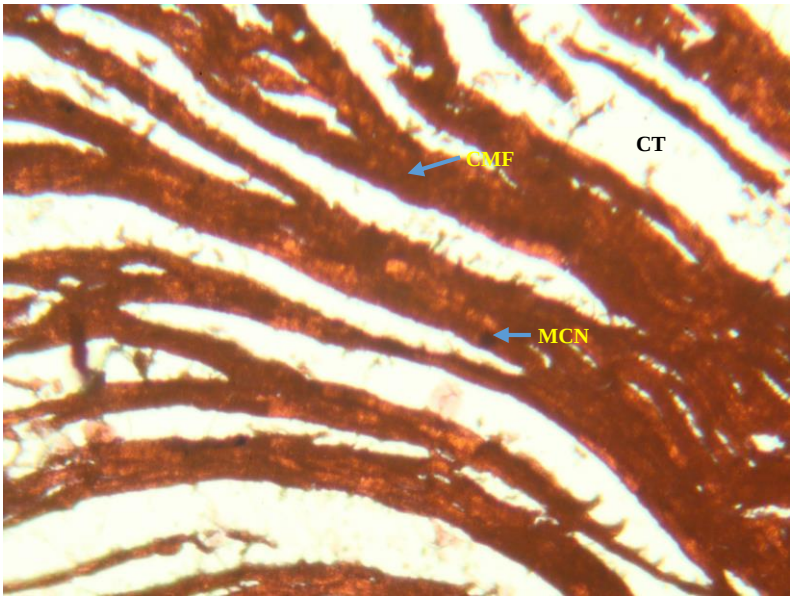



**Figure 42:** histological section of the heart treated with traditional yeast for 21 days Heamatoxylin - eosine staining (G×100).

MCN: muscle cell nucleus, CMF: cardiac muscle fibers, CT: connective tissue

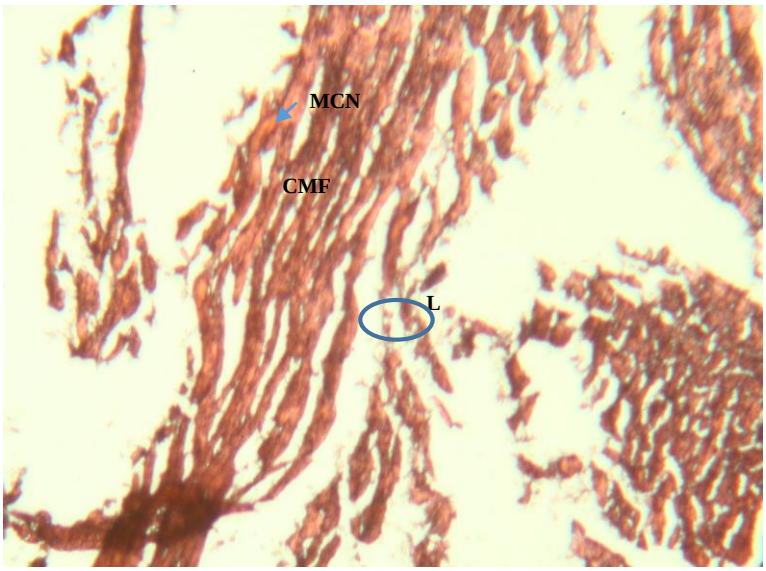



**Figure 43:** histological section of the heart treated with refined crystallize sugar and hot water for 21 days, Heamatoxylin - eosin staining (G×100).

MCN: muscle cell nucleus, CMF: cardiac muscle fibers, L: lysis.

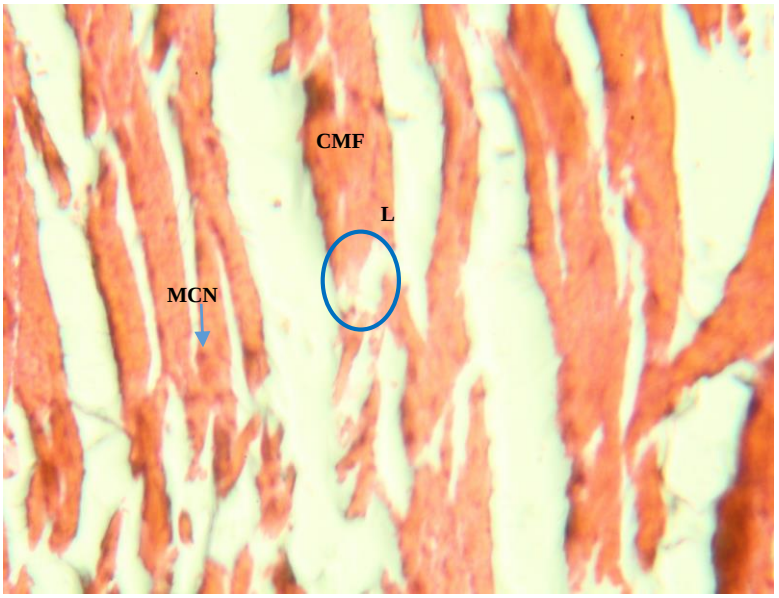



**Figure 44:** histological section of the heart treated with traditional yeast and refined traditional sugar for 21 days, Heamatoxylin - eosin staining (G×100).

MCN: muscle cell nucleus. CMF: cardiac muscle fibers.L: lysis.

## V. 2. 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 artificially sweetened 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 refined crystallized sugar on some biochemical parameters (CRP, Total-cholesterol, triglyceride, HDL-C, LDL-C, blood glucose and creatinine) and on the histological structure of the heart in mice.

### V. 2. 1. Body weight and food

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 obtained the the food consumed by mice is increased in the three groups, control group fed with standard diet, group treated with hot water and group fed with crystallize sugar during 21days of experimental study.

We detected in our study 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 study of 21days.

On the other hand, the quantity of food taken by animals is decreased in group fed with diet rich with traditional yeast and refined crystallize sugar this is an original work never done before.

### V. 2. 2. Biochemical investigations

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 **(Yanget 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 treated with hot water.

Total cholesterol as a risk factor for coronary heart disease (CHD) and stroke in women compared with men.

Raised total cholesterol is a strong risk factor for cardiovascular disease (CVD). It remains unknown whether sex differences exist in the relationship between total cholesterol and CVD outcomes **(Peterset al., 2016)**.

Epidemiologic studies provide evidence of an association between triglycerides and the development of primary CHD independently of HDL-C. Evidence of an inverse relationship between triglycerides and HDL-C suggests that both should be considered in CHD risk estimation and as targets for intervention **(Morrison and Hokanson, 2009)**.

We detected in this research, mice administered with refined crystallize sugar (200g/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 (50g/65kg).The concentration of T-CH is increased in group S this result is agree with the 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 group TYand decreased in TY+S

CRP as a mediator of disease **(Yeh, 2004)**. Coronary vascular disease (CVD) has a high prevalence in the United States, yet 40–50% of those with that diagnosis have normal or mildly increased cholesterol levels. Increased C-reactive protein (CRP) has been associated with CVD, in those presenting after an acute coronary event **(Farranti and Rifai, 2002)**.

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 hot water and traditional yeast.

Creatinine has been associated with increased mortality in hypertensive persons, the elderly, and patients with myocardial infarction or stroke in whom cardiovascular disease is the major cause of death **(Wannamethee et al., 1997)**.

The creatinine levels are increased in the group fed with refined crytallize 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**(Cai et al., 2022)**.

The underlying mechanisms of the association between ASAT and the risk for CVD or mortality are mostly hypothetical. It is important to note that there is no conclusive evidence that ASAT activity in serum parallels ASAT activity within the cells. Although, transamination is a fundamental reaction in the metabolism, a direct link between metabolic derangement associated with high or low ASAT levels and CVD remains largely unexplored. Furthermore, there are no known specific physiological function of ASAT in circulation outside the function as constituent of plasma proteins. Thus in order to explain the risk associated with ASAT, attention should be focused on underlying morbid conditions that are associated with high or

low ASAT levels. For ease of presentation, putative mechanisms linking high and low ASAT levels with CVD or mortality are analyzed separately **(Ndrepepa, 2021)**.

From our results we found that the liver enzymes (ASAT) are decreased in groups of the experimental study (S+HW, TY and S+TY) 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 originaland for this reason more study is needed in this part.

Glutathione (GSH), a naturally occurring thiol tripeptide 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.

### V. 2. 3. Histological study

Hot water treatment exerts a corrective effect on structural abnormalities of the heart. As the microscopic observation of the group (Hw+S) showed less damaged in muscle fibers than the group treated with sugar (S). Our results agree with the work of Boufedeche et al (2018), who reached that the hot water have a corrective effect on the structural anomalies of the heart.

Microscopic observation of mice treated with traditional yeast showed organized muscle fibers, while the group (S+TY) and the group (S+Hw) showed partial lysis of muscle fibers.

The use of traditional yeast alone does not have negative side effects on the heart, and helps reduce inflammatory markers and blood sugar levels, so traditional yeast protects the body from heart disease, atherosclerosis, and inflammation.

Regular drinking of hot water helps control the symptoms of high blood sugar levels and prevent their exacerbation. But there is not enough research to support the idea that hot water is a cure.

Bread made with traditional yeast is a good source of energy and nutrition, as traditional yeast can help in losing weight if used correctly and may help regulate and lower blood sugar in diabetics.

Histological investigation showed that the group of mice fed with high refined sugar has some lesion on the heart this was observed through the lysis and alterations in the cardiomyocytes. This alteration is due to the high level of low density lipoprotein (LDL-C). In contrast to the group control and treated with hot water and also the group treated with yeast observed that the heart has regular muscular fiber.

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

# Conclusion

## Conclusion

Heart diseases and atherosclerosis are among the diseases that need to search for and develop new treatments.

During thiswork, we have studied the effect of drinking hot water and eating traditional yeast on heart disease.

Many researchers have demonstrated that high consumption of crystallized sugar causes many diseases, hypertension, hyperlipidemia, and obesity. Which in turn causes heart disease and atherosclerosis. In this thesis, we dealt with natural treatment methods that help reduce the risk of inflammatiion in these diseases.

The results also showed that sugar consumption has an effect on the LDL-C and the lipids status in the blood, as well as the increase in the level of sugar in the blood, which may accelerate the incidence of atherosclerosis and heart problems.

Based on this thesis, we concluded that hot water has a positive effect on reducing weight and adjusting blood sugar. And thus contribute in reducing the risk of heart disease and arteries.

Traditional yeast has no side effects. But eating it with high amounts of sugar causes high blood sugar, according to the results of the experiment.

In the future, our research needs more studies to:

- Evaluate the effect of drinking hot water on blood sugar in human.
- Evaluate the effect of drinking hot water on cardiovascular diseaseand atherosclerosis in human.
- Evaluate the effect of traditional yeast on vitamins and minerals absorption.
- Evaluate the contribution of traditional yeast to metabolism.
- Evaluate the effect of traditional yeast treatment onthe digestive system diseases.
- Evaluate the effect of traditional yeast on blood sugar.

# References

## Reference

**Abderrahmne K., Seraoui R., and Nasri B**. (2022). Interaction between hot water and high consumption of crystallize sugar in cardiovascular disease. Thesis submitted for the degree of Master II. *University des frères Mentouri Constantine1 (Algeria).*

**Adamczyk-Sowa M., Sowa P., Mucha S., Zostawa J., Mazur B., Owczarek M., and Pierzchała K.** (2016). Changes in serum ceruloplasmin levels based on immunomodulatory treatments and melatonin supplementation in multiple sclerosis patients. *Medical Journal of Experimental and ClinicalResearch*, 22: 2484–2491.

**Ahnen R. T., Mottet R., Omolo M., and Slavin J.** (2020). Carbohydrates. Present Knowledge in Nutrition. *Present Knowledge in Nutrition (Eleventh Edition)*, 1: 37-50.

https://doi.org/10.1016/B978-0-323-66162-1.00003-2 ISBN: 9780128198421

**Albagli G., Finotelli P. V., Ferreira T. F., and Priscilla F. F. Amaral P. F. F.** (2023). Toward sourdough microbiome data: a review of science and patents. *Foods*, 12(2): 1-21.

**Aldairi A. F.** (2020). Evaluation of various methodologies used in purification of biologically active carbohydrates derived from marine life. *Biomedical Journal of Scientific & Technical Research*, 27(4): 20919-20927.

**Alhadjri F.** (2010). The miracle and wonders of treatment from hot water: hot water miracle.1-108.

**AlHajri F**. (2020). Corona- virus (COVID) out break and the last treasure. A*uthorHouse™ UK Bloomington*, USA.

**Amr A. S., and Alkhamaiseh A. M.** (2022). Sourdough use in bread production. *Jordan Journal of Agricultural Sciences*, 18(2): 81-98.

**Andersson B.** (1978). Regulation of water intake. *Physiology*, 58: 582-603.

**Aoki T., and Narumiya S.** (2012). Prostaglandins and chronic inflammation. *Pharmacological-sciences*, 33(6): 304-311.

**Arackal A., and Alsayouri K.** (2019). Histology, heart. StatPearls Publishing, Treasure Island. PMID: 31424727

**Araújo J. A, and Lusis A. J.** (2004). Atherosclerosis. *Encyclopedia of Endocrine Diseases (Second Edition)*, 1: 282-288. ISBN: 978-0-12-812200-6

**Asif H. M., Akram M., Saeed T., Khan M. I., Akhtar N., Riaz U. R., Ali Shah S. M., Khalil A., Shaheen G.** (2011). Carbohydrates. *International research journal of biochemistry and bioinformatics*, 1(1): 1-5.

**Bahadorfar M.** (2014). A study of hydrotherapy and its health benefits. *International Journal of Research*, 1(8): 294-305.

**Bakose R. Y, Al-Obaidi A. D., Al-Obaidi M. N., Al-Abbasi H., AL-Bayati M. O., Hashim A. T., Muhanned A., Alhaideri A., and Al-Dabagh J. D**. (2023). Anatomy of the Heart. *Heart Transplantation*, 1-17. DOI:10.1007/978-3-031-17311-0_1

**Barros V. N.** (2019). The heart cycle: review. *MOJ Womens Health*, 8(1): 66–69.

**Behera S. S., and Ray R. C.** (2015). Sourdough Bread. CRC Press, Boca raton, USA. Cristina M. Russell. 53-67.

**Bender T., Karagulle Z., Balint G. P., Gutenbrunner C., Balint P. V., and Sukenik S.** (2005). Hydrotherapy, balneotherapy, and spa treatment in pain management. *RheumatologyInternational*, 25: 220–224.

**Bhardwaj B., O'Keefe E. L., and O'Keefe J. H.** (2016). Death by Carbs: Added Sugars and Refined Carbohydrates Cause Diabetes and Cardiovascular Disease in Asian Indians. *The journal of Missouri State Medical Association*, 113(5): 395-400.

**Binjamini E., Sunshine G., and Leskowitz S.** (1996). Immunology a short course. Wiley-Liss, Ine. 605 Third Avenue, New York, NY10158-0012: 25-27.

**Boncler M., Wu Y., and Watala C.** (2019). The Multiple Faces of C-Reactive Protein-Physiological and Pathophysiological Implications in Cardiovascular Disease. *Molecules*, 24(11): 2062. Doi: 10.3390/molecules24112062

**Boufedeche S., Grendou Y., and Merikhi.F**. (2018). Effet de l'eau chaude sur les maladies cardiovasculaires induites par l'hypercholestérolémie chez les rats. Thèse Master II. *Université des frères Mentouri Constantine1 Algeria*.

**Braunwald E.** (1971). Structure and function of the normal myocardium. *British Heart Journal*, 33: 3–8.

**Bray C., Bell L. N., Liang H., Haykal R., Kaiksow F., Mazza J. J., and Yale S. H.** (2016). Erythrocyte Sedimentation Rate and C-reactive Protein Measurements and Their Relevance in Clinical Medicine. *Wisconsin Medical Journal*, 115(6): 317-321.

**Bull B. S.,Caswell M., Ernst E., Jou J M., Kallner A., KoepkeJ A., Lewis S M., Lowe G D., Rampling M W., and Stuart J.** (1993). ICSH recommendations for measurement of erythrocyte sedimentation rate. International Council for Standardization in Haematology (Expert Panel on Blood Rheology). *Journal Clinical Pathology*, 46(3): 198-203.

**Bunning M., Shackelton E., Pennington A., and Clark C.** (1908). Understanding and selecting sourdough for health benefits. *Colorado State University Extension*,

**Cai X. Y, Nan-Hui Z, Yi-Chun C, Shu-Wang G.** (2022). Sugar-sweetened beverage consumption and mortality from chronic kidney disease: results from the US .National Health and Nutrition Examination Survey. *Clinical Kidney Journal*, 15(4): 718-726.

**Calabro P., Golia E., and Yeh E T.** (2012). Role of C-reactive protein in acute myocardial infarction and stroke: possible therapeutic approaches. *Current Pharmaceutical Biotechnology*, 13(1): 4-16.

**Calvert M. D., Madden A. A., Nichols L. M., Haddad N. M., Lahne J., Dunn R. R., Erin A., and McKenney E. A.** (2021). A review of sourdough starters: ecology, practices, and sensory quality with applications for baking and recommendations for future research. *PeerJournal*, 9: 1-37.

**Carbonetto B., Nidelet T., Guezenec S., Perez M., Segond D., and Sicard D.** (2020). Interactions between *Kazachstania humilis* Yeast Species and Lactic Acid Bacteria in Sourdough. *Microorganisms*, 8(2): 240.

**Charitos E. I ., and Sievers H. H.** (2013). Anatomy of the aortic root: implications for valve-sparing surgery. *Annals of cardiothoracic surgery*, 2(1): 53.

**Chatterjee K., and Massie B.** (2007). Systolic and Diastolic Heart Failure: Differences and Similarities. *Journal of cardiac failure*, 13(7): 569-576. Doi: 10.1016/j.cardfail.2007.04.006

**Chowdhury R. S., Islam M. D., Akter K., Sarkar M. A. S., Roy T., and Tajdit R. S. M.** (2021). Therapeutic aspects of hydrotherapy: a review. *Bangladesh Journal of Medicine*, 32(2): 138-141.

**Coussens L. M., and Werb Z.** (2002). Inflammation and cancer. *Nature*, 420: 860–867.

**Cummings J. H., and Stephen A. M.** (2007). Carbohydrate terminology and classification. *European Journal of Clinical Nutrition*, 61: 5-18.

**Curtis M. J.** (1992). "The Heart and Cardiovascular System". *Cardiovascular Research*, 26 (7): 720.

**D'angelo G.** (2013). Role of hepcidin in the pathophysiology and diagnosis of anemia. *Blood Research*, 48: 10-15.

**Dahlqvist A., and Borgstrom B.** (1961). Digestion and Absorption of Disaccharides in Man. *Biohemical Journal*, 81: 411.

**Davis F J., Vidyasagar S., and Maiya G A.** (2012). C-reactive protein and coronary heart disease - risk marker or risk factor?. *Journal of Clinical Science Research*, 1: 178-186.

**De Vuyst L., Comasio A., and Kerrebroeck S. V.** (2021). Sourdough production: fermentation strategies, microbial ecology, and use of non-flour ingredients. *Food Science and Nutrition*, 63(15): 2447-2479.

**De Vuyst L., Harth H., Kerrebroeck S. V., Leroy F.** (2016). Yeast diversity of sourdoughs and associated metabolic properties and functionalities. *InternationalJournal of Food Microbiology*, 239(19): 26-34.

**Devkate G. V., Tate S. S., Deokate S. B., Bhujba A. S., Tupe A. P., and Patil R. N.** (2016). Hydrotherapy A New Trend in Disease Treatment. *Human Journals*, 5(2): 117-135.

**Douglas G., and Channon K. M**. (2014). The Pathogenesis of Atherosclerosis. *Medicine*, 42 (9): 480-484.

**Du W. C. T.** (2000). Function of C-reactive protein. *Annals of Medicine*, 32(4): 274-278. Doi: 10.3109/07853890009011772.

**Enríquez A., Calder V., Gao J., Galatowicz G., García-Vázquez C., Fernández I., Stern M. E., Diebold Y., and Calonge M.** (2008). Cytokine responses by conjunctival epithelial cells: An *in vitro* model of ocular inflammation. *Sytokin*, 44(1): 160-167.

**Erridge C.** (2008). The roles of pathogen-associated molecular patterns in atherosclerosis. *Trends in cardiovascular medicine*, 18(2): 52-56.

**Fam A. G., and Rheumatol J.** (1991). Spa treatment in arthritis: A rheumarologist's view. *Journal of Rheumatology*, 18: 1775–1777.

**Farranti S., and Rifai N.** (2002). C reactive protein and cardiovascular: review of risk prediction and intervention. *ClinicaChimicaActa*, 317(1-2): 1-15.

**Feehan K. T., and Gilroy D. W.** (2019). Is resolution the end of inflammation?. *Trends in molecular medicine*, 25(3): 198–214.

**Fukuta H., and Little W. C.** (2008). The cardiac cycle and the physiologic basis of left ventricular contraction, ejection, relaxation, and filling. *Heart failure clinic*s, 4(1): 1-11.

**Giudice D. E., Elia V., and Tedeschi A.** (2009). The role of water in the living organisms. *Neural Network World*, 19(4): 355-360.

**Glasser S. P., Selwyn A.P., Ganz P**. (1996).Atherosclerosis: Riskfactors and the vascular endothelium.*American Heart Journal*,131(2):379-384.

**Gulati S., and Misra A.** (2014). sugar intake, obesity, and diabetes in india. *Nutrients*, 6(12): 5955-5974.

**Hall J., Swinkels A., Briddon J., and McCabe C. S.** (2008). Does aquatic exerciserelieve pain in adults with neurologic or musculoskeletal disease? A systematic reviewand meta-analysis of randomized controlled trials. *Archives of physical medicine and rehabilitation*, 89: 873–883.

**Hawiger J.,and Zienkiewicz J.** (2019). Decoding inflammation, its causes, genomic responses, and emerging countermeasures. *Scandinavian journal of immunology*, 90(6): 1-32.

**Hegele R. A**. (1996). The pathogenesis of atherosclerosis. *Clinical Chimisty Acta*, 246(1-2): 21-38. Doi: 10.1016/0009-8981(96)06224-9

**Howard B. V., and Wylie-Rosett J.** (2002). Sugar and cardiovascular disease: a statement for healthcare professionals from the committee on nutrition of the council on nutrition, physical activity, and metabolism of the American heart association. *Circulation*, 106(4): 523-527.

**Italiani P and Boraschi D.** (2014). From monocytes to M1/M2 macrophages: phenotypical vs. functional differentiation. *Frontiers in Immunology*, 5(514): 1-22.

**Jenkins D. J., Wolever T. M., Taylor R. H., Barker H., Fielden H., Baldwin J. M., Bowling A. C., Newman H. C., Jenkins A. L., and Goff D. L.** (1981). Glycemic index of foods:a physiological basis for carbohydrate exchange. *The American Journal of Clinical Nutrition*, 34(3): 362–366.

**Joshi A H.** (2015). Rulebooks of drinking the water. 31(121): 134-136.

**Kamal M. A., and Klein P.** (2011). Determination of sugars in honey by liquidchromatography. *Saudi journal of biological sciences*, 18(1): 17-21.

**Kapellos T. S., Bonaguro L., Gemünd I., Reusch N., Saglam A., Hinkley E. R., and Schultze J. L.** (2019). Human monocyte subsets and phenotypes in major chronic inflammatory diseases. *Frontiers in immunology*, 10(2035): 1-13.

**Kezer G.** (2022). Functional perspective on sourdough bread. *Agriculture - Food Science and Technology*, 10(8): 1410-1414.

**Koivistoinen P., and Hyvönen L.** (1985). The use of sugar in foods. *International Dental Journal*, 35(3): 175-9.

**Kullo I. J., Gau G.T., Tajik A. J**. (2000). Novel risk factor for atherosclerosis. *Mayo Clinic Proceedings*, 75(4):369-380. Doi: 10.4065/75.4.369.

**Landis E. A., Oliverio A. M., McKenney E. A., Nichols L. M., KfouryN., Biango-Daniels M., Shell L. K., Madden A. A., and Shapiro L.** (2021). The diversity and function of sourdough starter microbiomes. *eLife Sciences*, 10(6): 1-24.

**Lau S. W., Chong A. Q., Chin N. l., Talib R. A., and Basha R. K.** (2021). Sourdough microbiome comparison and benefits. *Microorganisms*, 9(7):1355.

**Lee Y., Kumar S., Kim S. H., Seong K. Y., Lee H., Kim C., Jung Y. S., and Seung Y. Y.** (2020). Odorless glutathione microneedle patches for skin whitening. *Pharmaceutics*, 12(2): 100.

**Libby P., Buring J. E., Badimon L., K Hansson G., Deanfield J., Bittencourt M. S., Tokgözoğlu L., Lewis E.F**. (2019). Atherosclerosis. *Nature Reviews*, 5(1): 56.

Doi: https://doi.org/10.1038/s41572-019-0106-z

**Liu J., Zhang X., Cheng Y., and Cao X.** (2021). Dendritic cell migration in inflammation and immunity. *Cellularand molecular immunology*, 18: 2461–2471.

**Lobo A. J., Jones S. C., Juby L. D., and Axon A. T.** (1992). Plasma viscosity in inflammatory bowel disease. *Journal of clinical pathology*, 45(1): 54-57.

**Ludwig R. P.** (2001). Water: From clusters to the bulk. *Angewandte chemie*, 40(10):1808-1827.

**Lugrin J., Rosenblatt-Velin N., Parapanov R., and Liaudet L.** (2013). The role of oxidative stress during inflammatory processes. *Biological Chemistry*, 395(2): 203-230.

**Ma X., Nan F., Liang H., Shu P., Fan X., Song X., Hou Y., and Zhang D.** (2022). Excessive intake of sugar: An accomplice of inflammation. *Frontiers in* i*mmunology*, 13: 1-12.

**Mackiewicz A., and Mackiewicz K.** (1995). Glycoforms of serum Alpha 1-acid glycoprotein as markers of inflammation and cancer. *Glycoconjugate journal*, 12: 241-427.

**Marcus Y.** (2009). Effect of ions on the structure of water: structure making and breaking. *ACS Chemicalreviews*, 109(3): 1346-1370.

**McDowell R. E., Moody E. G., Van Soest P. J., Lehmann R. P., and Ford G. L.** (1969). Effect of heat stress on energy and water utilization of lactating cows. *Journal ofdairy science*, 52: 188-194.

**Meisner M.** (2014). Update on procalcitonin measurements. *Clinical Chemistry*, 34(4): 263-273.

**Melnikov I., Kozlov S., Saburova O., Avtaeva Y., Guria K., and Gabbasov Z.** (2023).Monomeric C-Reactive Protein in Atherosclerotic Cardiovascular Disease: advances and perspectives. *International Journal of Molecular Sciences*, 24(3): 2079.

**Mohammed A. S. A., Naveed M., and Jost N.** (2021). Polysaccharides: classification, chemical properties, and future perspective application in fields of pharmacology and biological medicine (A Review of current applications and upcoming potentialites). *Journal of Polymers and the Environment*, 29(8): 2359-2371.

**Moldoveanu B., Otmishi P., Jani P., Walker J., Sarmiento X., Guardiola J., Saad M., and Jerry Y.** (2022). Inflammatory mechanisms in the lung. *Journal of Inflammation Research*, 2: 1-11.

**Monastero., and Pentyala.** (2017). Cytokines as biomarkers and their respective clinical cutoff levels. *International Journal of Inflammation*, 2017: 1-11.

**Mondal S.** (2017). Chemistry of carbohydrates. *Pharm v sem applied biochemistry*, 1-19. Doi:10.13140/RG.2.2.32509.67040

**Mooventhan A., and Nivethitha L.** (2014). Scientific evidence-based effects of hydrotherapy on various systems of the body. *NorthAmerican Journal of Medical Sciences*, 6(5): 199-209.

**Morrison A., and Hokanswon J. E.** (2009). The independent relationshipbetween triglycerides and coronary heart disease. *Vascular health and risk mangement*, 5: 89-95.

**Mottl M. J. Glazer B. T., Kaiser R. I., and Meech K. J.** (2007). Water and astrobiology. *Geochemistry*, 67(4): 253-282.

**Mukai K., Tsai M., and Galli S. J.** (2018). Mast cells as sources of cytokines, chemokines and growth factors. *Immunological reviews*, 282(1): 121-150.

**Murakami M., and Hirano T.** (2012). The molecular mechanism of chronic inflammation development. *Frontiers in Immunology*, 3: 1-2. Doi: 10.3389/fimmu.2012.00323

**Muriel P., López-Sánchez P., and Ramos-Tovar E.** (2021). Fructose and the liver. *International Journal of Molecular Sciences*, 22(13): 6969.

**Ndrepepa G.** (2021). Aspartate aminotransferase and cardiovascular disease - a narrative review. *Journal of laboratory and precision Medcine*, 6(6): 1-17.

**Nehring S. M., Goyal A., and Patel B. C.** (2017). C reactive protein. Stat Pearls Publishing. Treasure Island (FL). PMID: 28722873

**Ngamchuea K., Christopher B. M., and Richard G. C.** (2017). Rapid method for the quantification of reduced and oxidized glutathione in human plasma and saliva. *American Chemical Society*, 85(5): 2901-2908. Doi: 10.1021/acs.analchem.6b04186

**O'Connor S., Taylor C., Campbell L. A., Epstein S., and Libby P.** (2001). Potential infectious etiologies of atherosclerosis: A Multifactorial perspective. *Emerging Infectious Diseases*, 7(5): 780-788.

**Olsson K., and Dahlborn K.** (1989). Fluid balance during heat stress in lactating goats. *Quarterly Journal*, 74: 645-659.

**Pahwa R., Goyal A., and Jialal I.** (2022). Chronic Inflammation. StatPearls Publishing, Treasure Island (FL). PMID: 29630225

**Pathak A.,and Agrawal A.** (2019). Evolution of C-reactive protein. *Frontiers Immunologie*, 10: 943. Doi: 10.3389/fimmu.2019.00943

**Peisajovich A., Marnell L., Mold C., and Du W. C. T.** (2008). C-reactive protein at the interface between innate immunity and inflammation. *Immunology*, 4(3): 379-390.

**Peters A. S., Singhateh Y., Mackay D., Huxley R. R., and Woodward M.** (2016). Total cholesterol as a risk factor for coronary heart disease and stroke in women compared with men: A systematic review and meta-analysis. *Atherosclerosis*, 248: 123-131.

**Pfützner A., Schöndorf T., Hanefeld M., and Forst T.** (2010). High-sensitivity C-reactive protein predicts cardiovascular risk in diabetic and nondiabetic patients: effects of insulin-sensitizing treatment with pioglitazone. *Journal Diabetes Scince Technology*, 4: 706-716.

**Pradhan A. D., Manson J. E, Rifai N., Buring J. E., Ridker P. M.** (2001). C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *Journal American Medical Association*, 286(3): 327-334.

**Punyauppa-path S., Kiatprasert P., Punyauppa-path P., Rattanachaikunsopon P., Khunnamwong P., Limtong S., and Srisuk N.** (2022). Distribution of kazachstania yeast in thai traditional fermented fish (Plaa-Som) in Northeastern Thailand. *Journal ofFungi*, 8(10): 1029.

**Rafieian-Kopaei M., Setorki M., Doudi M., Baradaran A., and Nasri H**. (2014). Atherosclerosis: Process, indicators, risk factor and new hopes. *International Journal of Preventive Medicine*, 5(8): 927-946.

**Raschke T. M.** (2006). Water structure and interactions with protein surfaces. *Current Opinion in Structural Biology*, 16(2): 152-159.

**Reddy M. S**. (2020). Steps of atherosclerosis and its complication. *Journal of Medical Pharmaceutical*, 2577-2579. Doi:10.22270/jmpas.v9i4.967

**Rehman I., Nassereddin A., and Rehman A.** (2022). Anatomy, thorex, pericardium. StatPearls Publishing, Treasure Island (FL). ID: NBK482256

**Rehman K ., and Akach M. S. H.** (2016). Mechanisms of inflammatory responses and development of insulin resistance: how are they interlinked?. *Journal of Biomedical Science*, 23(87): 1-18.

**Rodriguez E. R., and Tan. C. D.** (2017). Structure and anatomy of the human pericardium. *Progress in Cardiovascular Diseases*, 59(4): 327-340.

**Ross R**. (1993). The pathogenesis of atherosclerosis; a perspective for the 1990s. *Nature*, 362(6423): 801-809.

**Rosales C.** (2018). Neutrophil: A cell with many roles in inflammation or several cell types?. *Frontiers Physiology*, 9:113.

**Saitkulov F. E., Azimov I. O., Ergasheva M. A., Jo H. O., and Shaxabiddinova R. S.** (2022). Carbohydrates are the main source of energy in the body. *Solution of social problems in management and economy*, 7: 68-71.

**Salazar J., Martínez M. S., Chávez M., Toledo A., Añez R., Torres Y., Apruzzese V., Carlos S., Rojas J., and Bermúdez V.** (2014). C-Reactive Protein: clinical and epidemiological perspectives. *Cardiology Research and Practice*, 2014: 1-10.

**Sanada F., Taniyama Y., Muratsu J., Otsu R., Shimizu H., Rakugi H., and Morishita R.** (2018). Source of chronic inflammation in aging. *Frontiers in CardiovascularMedicine*, 5(12): 1-5.

**Sawka M. N., Cheuvront S. N., and Carter R.** (2005). Human water needs. *Nutrition Reviews*, 63(6): 30–39.

**Seeberger H. P.** (2017). Monosaccharide diversity. Cold spring harbor laboratory press, Cold Spring Harbor (NY). Doi: 10.1101/glycobiology.4e.2

**Shah P. K., and Lecis D.** (2019). Inflammation in atherosclerotic cardiovascular disease. *F1000Research*, 8: 1-10. Doi: 10.12688/f1000research.18901.1

**Sharp K. A.** (2001). Water: Structure and Properties. Johnson Research Foundation, University of Pennsylvania,Philadelphia, Pennsylvania, USA1-7. Doi:10.1038/npg.els.0003116

**Sherwood E. R ., and Toliver-Kinsky T.** (2004). Mechanisms of the inflammatory response. *Best practice and research clinical Anaesthesiology*, 18(3): 385–405.

**Shrivastava A. K., Singh H. V., Raizadaand A., andSingh S. K .** (2014). C-reactive protein, inflammation and coronary heart disease. *The Egyptian Heart Journal*, 67(2): 89-97.

Doi: https://doi.org/10.1016/j.ehj.2014.11.005

**Siswanti H., Yusra S, and Budiani S. (**2021). Hydrotherapy of Blood glucose level at time fordiabetes mellitus (DM) Patient. *Paris Van Java International Journal*, Doi: 10.2991/assehr.k.210304.150

**Sproston N. R and Ashworth J. J.** (2018). Role of C-reactive protein at sites of inflammation and infection. *Frontiers in Immunology*, 13(9): 754.

**Subaraman M.,Devi R. G., and Jothi P. A.** (2020). Knowledge and awareness about benefits of drinking hot water- a survey. *PalArch's Journal of Archaeology of Egypt / Egyptology*, 17(7): 1630-1638.

**Szabo A., Gogolak P., Koncz G., Foldvari Z., Pazmandi K., Miltner N., Poliska S., Bacsi A., Djurovic S., and Rajnavolgyi E.** (2018). Immunomodulatory capacity of the serotonin receptor 5-HT2B in a subset of human dendritic cells. *Scientific Reports*, 8: 1765.

**Tall A. R.** (2004). C-reactive protein reassessed. *New England Journal of Medicine*, 350(14): 1450-1452.

**Targońska S., and Majdan.** (2014). Serum amyloid A as a marker of persistent inflammation and an indicator of cardiovascular and renal involvement in patients with rheumatoid arthritis. *Mediators of Inflammation*, 2014: 1-7.

**Tegos T. J., Kalodiki E., Sabetai M. M., and Nicolaides A. N.** (2001). The Genesis of Atherosclerosis and Risk Factors. *Angiology journals*, 52(2): 89-98.

**Thacker E.** (2006). Lung inflammatory responses. *Veterinary Research*, 37(3): 469-486.

**Theoharides C. T., Alysandratos K. D., Angelidou A., Delivanis D. A., Sismanopoulos N., Zhang B., Asadi S., Vasiadi M., Weng Z., Miniati A., and Kalogeromitros D.** (2012). Mast cells and inflammation. *Biochimica et Biophysica Acta*, 1822(1): 21-33.

**Thiele J. R., Zeller J., Bannasch H., Stark G. B., Peter K., and Eisenhardt S. U.** (2015). Targeting C-Reactive protein in inflammatory disease by preventing conformational Changes. *Mediatorsof Inflammation*, 1-9.

**Thompson D., Pepys M. B., and Wood S. P.** (1999). The physiological structure of human C-reactive protein and its complex with phosphocholine. *Structure*, 7:169 –177

**Tillett W. S., and Francis T.** (1930). Serological reactions in pneumonia with a non-protein somatic fraction of pneumococcus. *The Journal of experimental medicine*, 52: 561–571.

**Verhagen S. N., and Visseren F. L. J.** (2011). Perivascular adipose tissue as a cause of atherosclerosis. *Atherosclerosis*, 214 (1): 3-10.

**Vermeire S,. Assche G. V., and Rutgeerts P.** (2004). C-Reactive protein as a marker for inflammatory bowel disease. *Frontiers*, 10(5) :661–665.

**Volanakis J. E.** (2001). Human C-reactive protein: expression, structure, and function. *Molecular Immunology*, 38(2-3): 189-197

**Wang Y. W., Kinzie1 E., Franklin G. B., Sai K. L., and Baumann1 H .** (2001). Haptoglobin, an inflammation-inducible plasma protein. *Redox Report*, 6: 379–385.

**Wannamethee S. G., Shaper A. G., and Parry I. J.** (1997). Serum creatinine concentration and risk of cardiovascular disease: a possible marker for increased risk of stroter. *Stroke*, 28(3): 557-563.

**Watson J, Round A, Hamilton W.** (2012). Raised inflammatory markers.*British medical journal*, 344: 454.

**Wright H. L., Moots R. J., Bucknall R. C., and Edwards S. W.** (2010). Neutrophil function in inflammation and inflammatory diseases. *Rheumatology*, 49(9): 1618-1631.

**Wu Y., Lawrence A., Potempa., El Kebir D., and János G. F.** (2015). C-reactive protein and inflammation: conformational changes affect function. *Biological Chemistry*, 396(11): 1181–1197.

**Xi B., Huang Y. B., Reilly K. H., Li S. S., Zheng R. L., and Barrio-Lopez M. T.** (2015). Sugar-sweetened beverages and risk of hypertension and CVD: a dose-response meta-analysis. *Britich Journal of Nutrition*, 113(5): 709-17.

**Xiao Feng Pang. (2014)**. Water: molecular structure and properties. USA Hackensack, NJ 07601, UK London WC2H9HE: Singapore.

**Yamazaki F., Endo Y., Torii R., Sagawa S., and Shiraki K.** (2000). Continuous monitoring of change in hemodilution during water immersion in humans: Effect of water temperature. *Aviation, Space, and Environmental Medicine*, 71: 632–639.

**Yang B., Glenn A. J., Liu Q., Madsen T., Allison M. A., Shikany J. M., Manson J. E., Hang K. K. C., Wen-Chih W., Li J., Liu S., and Kenneth L.** (2022). Added Sugar, Sugar-Sweetened Beverages, and artificially sweetened beverages and risk of cardiovascular disease: findings from the women's health initiative and a network meta-analysis of prospective studies. *Nutrients*, 14(20): 4226.

**Yang Q., Zhang Z., Gregg E. W., Flanders D., MA R. M., Hu F. B.** (2014). Added sugar intake and cardiovascular diseases mortality among US adults. *JAMA Internal Medicine*, 174(4): 516-524.

**Yeh E. T. H.** (2004). CRP as a mediator of disease. *Circulation*, 109(21): 11-14.

**Yu Y., Shen M., Song Q., and Xie J.** (2017). Biological activities and pharmaceutical applications of polysaccharide from natural resources: A review. *Carbohydrate Polymers*, 183: 91-101.

**Zaitoun M., Maissam Ghanem M., and Harphoush S.** (2018). Sugars: types and their functional properties in food and human health. *International Journal of Public Health Research*, 6(4): 93-99.

**Zhao H., Wu L., Yan., Chen Y., Zhou M., Wu Y., and Li Y.** (2021). Inflammation and tumor progression: signaling pathways and targeted intervention. *Signal Transduction and Targeted Therapy*, 6(263): 1-46.

**Reference Site Web**

**Ball J.** (2022). Is sourdough bread healthy?. *Eating well*,

https://www.eatingwell.com/article/7904008/health-benefits-of-sourdough-bread-according-to-a-dietitian/

**Belleza M.** (2023). Cardiovascular System Anatomy and Physiology. *Nurseslabs*,

https://nurseslabs.com/cardiovascular-system-anatomy-physiology/

**Blackwood M.** (2022). Health benefits of sourdough bread. *Healthier steps*,

https://healthiersteps.com/health-benefits-of-sourdough-bread/

**Kohli P.** (2020). The heart: All you need to know. *Medical News Today*,
https://www.medicalnewstoday.com/articles/320565

**Lennon A.** (2023). Cardiovascular disease: Added sugars may increase risk. Medicalnewstoday,
https://www.medicalnewstoday.com/articles/cardiovascular-disease-risk-added-sugars-dietary-fiber

**Marengo K.** (2019). Does sugar cause inflammation in the body?. *Medical News Today*.

https://www.medicalnewstoday.com/articles/326386

**Marengo K.** (2023). What are the benefits of nutritional yeast?. *Medical news today*,

https://www.medicalnewstoday.com/articles/323245

**McGruther J.** (2022). Easy Sourdough Starter. *Nourished kitchen*,

https://nourishedkitchen.com/how-to-make-a-sourdough-starter/

**Rogalskyi V.** (2022). Coronary arterial dominance. *Radiopaedia*,

https://radiopaedia.org/articles/coronary-arterial-dominance

**Weerakkody Y.** (2023). Coronary veins. *Radiopaedia*,

https://radiopaedia.org/articles/coronary-veins

1. https://www.nicepng.com/ourpic/u2e6y3e6w7e6a9a9_cho-map-polysaccharide-concept-map/
2. https://www.shutterstock.com/fr/image-vector/chemical-illustration-monosaccharides-glucose-fructose-galactose-2211684449
3. https://www.shutterstock.com/fr/image-vector/chemical-illustration-disaccharides-maltose-sucrose-lactose-2211686407
4. https://o.quizlet.com/lCUXmdUt0vRwxu3PhOyfPw.png
5. https://content.byui.edu/file/a236934c-3c60-4fe9-90aa-d343b3e3a640/1/module3/images/polysaccharides2.png
6. https://nutrition.org/inflammation-what-is-it-and-how-can-my-diet-and-behavior-affect-it/
7. https://nurseslabs.com/cardiovascular-system-anatomy-physiology/
8. https://heart.thecommonvein.net/structure/histology-
   https://www.getbodysmart.com/heart-anatomy/pericardium/
9. https://www.researchgate.net/figure/Histologic-section-of-a-normal-myocardium-of-a-control-case-Arrows-shows-normal-muscle_fig6_313819702
10. https://www.researchgate.net/figure/Different-stages-in-progression-of-atherosclerosis-8_fig1_308414603
11. https://www.differencebetween.com/what-is-the-difference-between-hypertension-and-atherosclerosis/
12. https://www.istockphoto.com/fr/vectoriel/athérosclérose-gm835897628-135950383
13. https://study.com/learn/lesson/properties-water-structure-density-molecules.html
14. https://fos.cmb.ac.lk/blog/freezes-faster-warm-water-cold-water/

# Summary

**Summary**

There is a close relationship between excess sugar consumption and heart disease. Prolonged high blood sugar can damage blood vessels, increasing the risk of heart disease.

High blood sugar causes damage to blood vessels and high cholesterol, which weakens the perfusion of the heart muscle and raises pressure to add another burden on the heart.

In the present study, we evaluated *in vivo* the interaction of high consumption of refined crystallize sugar (200mg/kg) , hot water at 50°C and the traditional yeast on the heart 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 heart.

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 an ameliorations on the heart tissue by the treatment with yeast and hot water.

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 heart inflammation
**Keywords:** inflammation, heart, glutathione reduced, lipids profile, ASAT, ALAT

**Résumé**

Il existe une relation étroite entre la consommation excessive de sucre et les maladies cardiaques. Une glycémie élevée prolongée peut endommager les vaisseaux sanguins, augmentant le risque de maladie cardiaque.

Une glycémie élevée provoque un taux de cholestérolélevé, ce qui affaiblit la perfusion du muscle cardiaque et augmente la pression pour ajouter un autre fardeau sur le cœur.

Dans notreétude, nous avonsé value *invivo* l'interaction du sucre cristallisé et de l'eau chaude à 50°C et de la levure traditionnelle sur le coeur pendant 21 jours de traitement 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 ducoeur. Les résultats ont indiqué que l'utilisation d'eau chaude à une température de 50 °C avait la capacitéd'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 consummation de la levure traditionnelle réduit la CRP, la creatinine et les enzymes hépatiques et augmente la concentration de HDL-C. Nous avons observé des ameliorations sur le tissue cardiaque par le traitement à la levure et à l'eau chaude.

Nous avons conclu que l'eau chaude à une température de 50°C et une consummation de la levure traditionnelle peut être considérée comme une mesure preventive naturelle pour réduire l'inflammation cardiaque.

**Mot clés**: inflammation, coeur, glutathione réduit, profillipidique, ASAT, ALAT

**الملخص**

هناك علاقة وثيقة بين الافراط في تناول السكر و امراض القلب'.يمكن ان يؤدي ارتفاع نسبة السكر في الدم لفترات طويلة الى تلف الاوعية الدموية، مما يزيد من خطر الاصابة بامراض القلب.

ان ارتفاع سكر الدم يؤدي الى إرتفاع الكولسترول مما يضعف تروية عضلة القلب ويرفع الضغط ليضيف عبئ آخر على القلب .

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. تم تقييم ذلك باستخدام الكشف عن الجلوكوز في الدم ، الدهون ، الجلوثاثيون المختزل' الكريلتنين'البروتين سي التفاعلي و فحص قطاعات نسيجية على القلب.

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.

استهلاكالخميرة التقليدية تقلل من بروتين سي التفاعلي والكرياتينين وأنزيمات الكبد و تعمل على زيادة تركيز HDL-C.

لاحظنا تحسنًا في النسيج القلبي من خلال العلاج بالخميرة والماء الساخن.

وهكذا توصلنا إلى أن الماء الساخن عند درجة حرارة 50 درجة مئوية و استهلاك الخميرة التقليدية يمكن ان يكون واقيا لالتهابالقلب.

**الكلمات المفتاحية:**الالتهابات'القلب ' الجلوتاثيون المختزل 'الليبيدات' انزيمات كبدية

# Annex

# 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 at 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 of sulphosalic acid**

0.25g Sulphosalic acid ⟶ 100ml distilled water.

- **Preparation of Tris EDTA**

6.06g tris + 0.96g EDTA ⟶ 125ml distilled water ⟶ pH= 9.6 (modified by HCl.

- **Preparation of Bouin alcohol**

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 hematoxylin ⟶ 10 ml distilled water

- **Preparation of eosin**

2 g eosin ⟶ 100ml distilled water

- **Preparation of gelatin**

0.5 g gilatin ⟶ 100 ml distilled water

**Table 05:** 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 06:** composition of standard diet.

| 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 |

**Table 07:** calibration 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** | 5 | 5 | 5 | 5 | 5 | 5 |
| **DO** | 0 | 0.207 | 0.420 | 0.583 | 0.722 | 0.874 |

**Academic year** : 2022 :2023

**Presented by**: Boughachiche Zina
Bouzid Amira
Derouiche Maroua

# The effect of hot water and traditional yeast on the heart inflammation induced by refined crystallize sugar

**Thesis presented for the obtention of the degree of master II**

There is a close relationship between excess sugar consumption and heart disease. Prolonged high blood sugar can damage blood vessels, increasing the risk of heart disease.

High blood sugar causes high cholesterol, which weakens the perfusion of the heart muscle andraises pressure to add another burden on the heart.

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**Keywords :**inflammation, heart, glutathione reduced, lipids profile, ASAT, ALAT

**Research laboratory:** Université des frères Mentouri-Constantine 1, laboratory of Immunology