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Biological Activities and Nutritional Composition of *Rhus coriaria* L. (Sumac).

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M.Sc. Thesis

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Dedication

This thesis is dedicated to the enduring bonds of family, whose love and encouragement have illuminated my academic path. May this dedication reflect the deep gratitude and love I hold for each of you.

To the everlasting spirit of my father, whose unwavering presence – a constant source of strength – continues to inspire and guide me, even in his physical absence.

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List of Abbreviations

ABTS	2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid
apo	Apolipoprotein
aPTT	Activated partial thromboplastin time
BHA	Butylated hydroxyanisole
BHT	Butylated hydroxytoluene
CFU	Colony-forming unit
cm	Centimeter
COVID-19	Coronavirus disease 2019
COX	Cyclooxygenase
CUPRAC	Cupric reducing antioxidant power assays
DNA	Deoxyribonucleic acid
DPPH	2,2-diphenyl-1-picryl-hydrazyl-hydrate
ESBL	Extended Spectrum Beta-Lactamase
eNOS	Endothelial nitric oxide synthase
FRAP	Ferric reducing antioxidant power
GA	Gallic acid
GC-Ms	Gas chromatography-mass spectrometry
HbA1c	Glycosylated hemoglobin
HMEC-1	Human microvascular endothelial cells
HPLC–DAD–ESI-MS/MS	High-performance liquid chromatography-diode array detector-hyphenated with tandem mass spectrometry
HPLC-PDA	High-Performance Liquid Chromatography with Photodiode Array Detection
HUVEC	Human umbilical vein endothelial cell
IC_{50}	Half-maximal inhibitory concentration
Kcal	Kilocalories
MeOH	Methanol

mg g^{-1}	Milligram per gram
mg GAE/g dry weight	Milligrams of Gallic acid equivalents per gram of dried plant
MIC	Minimal inhibitory concentration
mm	Millimeter
MRSA	Methicillin-resistant Staphylococcus aureus
nm	Nanometer
PT	Prothrombin time
RNA	Ribonucleic acid
ROS	Reactive oxygen species
RT	Room temperature
TAC	Total antioxidant capacity
TNF	Tumor necrosis factor
UV	Ultraviolet
wt./vol	Weight per volume
µg/mL	Microgram per milliliter
°C	Celsius

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Abstract

Rhus coriaria L. (Anacardiaceae), commonly known as sumac, is a commonly used spice, condiment, and flavoring agent, especially in the Mediterranean region. Owing to its bountiful beneficial values, sumac has been used in traditional medicine for the management and treatment of many ailments including hemorrhoids, wound healing, diarrhea, ulcer, and eye inflammation. This plant is rich in various classes of phytochemicals including flavonoids, tannins, polyphenolic compounds, organic acids, and many others. This study presents a comprehensive exploration of the biochemical activities and potential therapeutic applications of *Rhus coriaria* (sumac) fruits, integral to Palestinian culinary heritage. Motivated by Sumac's widespread use in traditional Palestinian dishes and its potential as a functional ingredient, alongside the scarcity of studies on Palestinian Sumac extracts, Turkish Sumac was included for comparison. The overarching objective is to investigate and evaluate the biological activities and nutritional composition of *Rhus coriaria* fruits, specifically assessing antibacterial activities, antioxidant properties, total phenol contents, *in vitro* anticoagulation, HPLC-PDA analysis, proximate composition, and mineral estimation of Palestinian and Turkish-cultivated Sumac fruit extracts.

Findings demonstrate remarkable antibacterial efficacy for both Palestinian and Turkish Sumac against drug-resistant strains, specifically gram-positive MRSA with Palestinian extracts showing up to 95.65% inhibition and Turkish extracts showing up to 73.91%. Assessment of antioxidant properties and total phenol content reveals that reflux extraction using 100% methanol consistently demonstrates enhanced antioxidant potential in both Palestinian and Turkish Sumac. The superior efficacy of the 100% methanol reflux extraction method over 80% methanol and room temperature extraction methods can be attributed to the higher solubility and extraction efficiency of methanol at elevated temperatures, which enhances the release of phenolic compounds and other bioactive constituents responsible for the tested biological activities.

The study also investigates Sumac's potential as a natural anticoagulant. The findings reveal a significant ($P < 0.05$), concentration-dependent prolongation of activated

partial thromboplastin time (aPTT) by both Palestinian and Turkish Sumac extracts, indicating a specific influence on the intrinsic coagulation pathway while sparing the extrinsic pathway with Palestinian extracts prolonging aPTT up to 59.6 seconds and Turkish extracts up to 57.8 seconds. HPLC analysis identified shared compound profiles in Palestinian and Turkish extracts, including gallic acid and rutin, suggesting uniformity in biological activities.

Mineral analysis revealed that potassium was the most abundant mineral, with concentrations up to 6997 ppm, followed by calcium, with concentrations up to 3440 ppm, and magnesium, with concentrations up to 2959 ppm, Zinc was present in the lowest concentrations, measured at around 55.9 ppm. Proximate analysis reveals that both Palestinian and Turkish Sumac extracts are rich in fiber, followed by fat and moisture content.

Despite some variations, both sources share significant hemostatic potential and specific bioactive compounds, emphasizing their overall functional similarity. Minor differences in proximate parameters were noted, with Turkish Sumac showing higher fat content and lower moisture content. Mineral estimation showed no significant differences between Turkish and Palestinian Sumac extracts, underscoring their overall bioactivity and functional similarity.

Chapter One: Introduction

1. Introduction

The ancient aphorism by Hippocrates, "Let food be the medicine and medicine be the food," underscores the profound connection between culinary usage and potential health benefits. Over centuries, herbs and spices have attracted human attention, far beyond flavor enhancers but repositories of therapeutic properties. Recognizing their chemistry, active constituents, pharmacodynamics, and health-promoting attributes has reshaped their applications as well as a tapestry of interconnected culinary and medicinal use as well (Guiné and Gonçalves, 2015; Teodoro, 2019; Dixit *et al*., 2023). Indeed, people have used plants both as a source of food and remedies. This dual role persisted even when the active components of these plants were not fully understood, and their use was based on the observation of their efficacy to discover their therapeutic properties (Cowan, 1999; Petrovska, 2012).

In the cultural fabric of Palestine, herbal medicine holds a vital position in contemporary public health care, rooted back to Ancient Arab- Islamic medicine, influenced by the medical practices in Persia, Mesopotamia, Greece, Rome, and India (Abu Rabia, 2005). Due to Palestine's diverse geography and climate, the Palestinian mountains hosts over 2600 plant species of which more than 700 species are noted for their uses as medicinal herbs or botanical pesticides (Shawarb *et al*., 2023). However, scientific examinations of these medicinal plants, their efficacy, safety, toxicity, dosage, and usage instructions are limited, and they are almost always passed down verbally from one generation to another (Sawalha *et al*., 2008).

Among Palestine's botanical treasures is *Rhus coriaria* L., commonly referred to as Sumac, a member of the Anacardiaceae family, thriving in the Mediterranean region (Adwan *et al*., 2015). This wild shrub, holds culinary significance in the Eastern Mediterranean, particularly in Palestine, Lebanon, Syria, Jordan, Turkey, and Iran, Sumac's dried powdered fruits are a popular spice, adding a sour lemony taste to various dishes, feature prominently in Palestinian meals, most notably, Al-Musakhan and Za'atar (Abu-Reidah *et al*., 2014; Alsamri *et al*., 2021). Apart from culinary applications, Sumac historically played a role in leather tanning due to its high tannin content (Redwood, 2020).

Sumac's abundant benefits extend to traditional medicine, where its fruits have been employed to address a range of health issues including ulcers (Tuzlacı and Aymaz, 2001), diarrhea (Sezik *et al*., 2001; Said *et al*., 2002; Lev, 2002), liver disease, and urinary tract problems. Additionally, powdered fruits have been used to lower cholesterol levels and induce sweating (Lev, 2002). The diverse biological characteristics of *Rhus coriaria* contribute to its numerous medicinal benefits these include antibacterial, antifungal, anti-inflammatory, antioxidant, antiemetic, antidiarrheal, antiviral, anti-ischemic, cardiovascular protective, hypoglycemic, hypolipidemic, leukopenic, and antifibrinogenic properties (Beretta *et al*., 2009; Shabir, 2012; Abu-Reidah *et al*., 2014).

In addition, Sumac's richness in various classes of phytochemicals, such as flavonoids, hydrolysable tannins, polyphenolic compounds, organic acids, terpenoids, anthocyanins, and coumarin derivatives, further emphasizes it as a valuable resource in traditional medicine. Initial investigations in 1896 identified myricetin and gallic acid in its leaf extract (Perkin, 1896), while recent analyses identified 211 phyto-constituents in the fruit extract, with 180 characterized for the first time (Abu-Reidah *et al*., 2015). Advanced techniques like microwave-assisted extraction have increased the yield of Sumac oil, highlighting terpene hydrocarbons as primary components (Gharaei, 2013; Reidel, 2017). This rich phytochemical diversity within *Rhus coriaria* lays the groundwork for a comprehensive investigation into its therapeutic properties.

1.1. Problem Statement and Motivation of the Study

The current research represents the first exploration into the impact of Sumac extract on coagulopathy, driven by existing indications of its promising potential as a source of functional and nutraceutical ingredients. Given Sumac's widespread culinary use in Palestine and its emerging role as a functional ingredient, coupled with the scarcity of research on Palestinian Sumac, Turkish Sumac was included for comparison. This research focuses on evaluating the biological activities of *Rhus coriaria* L. with the aim of stimulating further exploration into its applications in food preservation, pharmacology, and the functional food industries.

1.2. Aim of the Study

The overarching objective of this study is to comprehensively investigate and evaluate the biochemical activities of *Rhus coriaria* fruits. This investigation encompasses

diverse aspects, including evaluating antibacterial, antioxidant, *in vitro* anticoagulation activities, and proximate and mineral composition of Palestinian and Turkish Sumac.

1.3. Objectives of the Study

1. To assess the *in vitro* anticoagulation potential of Sumac fruit extracts using prothrombin time and activated partial thromboplastin time tests.

2. To compare the biological activities, total ash, fiber, fat, and mineral content of Palestinian-cultivated Sumac with that of Turkish-cultivated Sumac.

3. To evaluate the *in vitro* antibacterial activities of Sumac extracts against two selected drug-resistant pathogenic bacterial strains: MRSA as a gram-positive strain, and ESBL as a gram-negative strain.

4. To assess the antioxidant activity of Sumac fruit extracts using ABTS●+ and DPPH● assays.

5. To identify the chemical components of phytochemical using HPLC analysis.

6. To determine the total phenol content using the Folin-Ciocalteu method.

7. To compare the biochemical activities of locally sourced and Turkish Sumac, employing two distinct extraction techniques: reflux extraction and room temperature extraction. Furthermore, a comparison will be conducted using two different solvent concentrations: 100% and 80% Methanol.

Chapter Two: Literature Review

2. Literature Review

2.1. Taxonomical classification of *Rhus coriaria* L.

Taxonomical classification (Abdul-Jalil, 2020)

Family: Anacardiaceae

Genus: *Rhus*

Species: *coriaria*

2.2. Etymology

The name "Sumac" originated from "summāq" which means "dark red" in Arabic. (Abu-Reidah *et al*., 2014). Also, from the Syriac word "Sumaga", which also translates to "red" (Quattrocchi, 1999). Sumac is the generic name of the *Rhus* genus, which comprises 91 accepted species in the Anacardiaceae family (Abu-Reidah *et al*., 2014). The Sumac name is applied to the spice product of the plant *Rhus coriaria*, which is also known as Tanner's Sumac or Sicilian Sumac in English.

2.3. Habitat and Distribution

Rhus coriaria wildly grows in the Mediterranean bordering countries, South Europe, North Africa, Iran, Iraq, Afghanistan, and Southeastern Turkey. The plant is also cultivated in temperate and tropical regions worldwide **(**Abdul-Jalil, 2020).

2.4. Botanical Description

Rhus coriaria grows as a shrub with a 3–4-meter height and has pinnate leaves arranged in pairs of 6 or 8 small leaflets, with a cluster of greenish, reddish, or creamy white flowers at the terminal inflorescences. The fruits are small (length 3.5–4.0 cm and width 2–2.5 cm) dark- brown, hard, spherical, hairy, and become reddish drupe when ripe, configuring dense clusters at branch tips, which called Sumac**, Figure 2.1**. The fruit has one hard, brown-colored seed (Abu-Reidah *et al*., 2014).

Figure 2.1: (A) *Rhus coriaria* plant and (B) *Rhus coriaria* fruit.

2.5. Sumac Cultivation

2.5.1. Climatic and soil requirements

Sumac is a tough plant that can adapt to almost any environmental condition. It can grow in poor, rocky soils with little access to water. And it does well in moderately dry or moist locations, whether the soil is acidic, alkaline, sandy, or clayey.

Sumac is highly adaptable to soil types, including overly sandy, rocky, clay, and shallow soil; the only caveat is drainage, so the soil must be able to drain adequately. (Huxley, A., 1992). It is also adaptable and handles a wide pH range from 4.5 to 7.5 without adverse effects. As well as they are light-loving trees, doing best in full sun to part shade.

Regarding temperature, Sumac trees can tolerate high temperatures that may reach 40C, and they tolerate cold and frost. Still, they prefer warm and temperate areas and are suitable for a maximum temperature of 20-35 C and a minimum temperature of 1-2 C.

Sumac is found in areas with rainfall ranges from 700-1000 mm/year. However, Sumac is a drought-tolerant plant that adapts to rains ranging from 200-300 mm/year. And it tolerates snow, winds, and dry climates.

2.5.2. Propagation of Sumac plant

Sumac trees can be propagated by stolons, root cuttings, cuttings, or by seed. The propagation of Sumac by seed requires scarifying the seeds using either mechanical methods or chemical scarification using concentrated sulfuric acid to stimulate germination.

Sumac can be propagated through seeds and rhizomes, and artificial propagation is carried out mainly using sprouts from rhizomes (Perrone *et al*., 2022).

2.6. The uses of *Rhus coriaria* L.

2.6.1. Culinary uses of Sumac

The fruits of Sumac can be used fresh to make tea, or more often it is dried, and ground to produce a tangy, red-purple powder popular in many countries as a culinary seasoning. It is used in combination with salt and onions as a seasoning for roast meat throughout the Mediterranean region.it is also used as a garnish on meze dishes such as hummus due to its attractive red color. As well as being one of the main ingredients in the Palestinian dish Al-musakhan. In addition, it is used in Za'atar, a mixture of dried thyme with Sumac and sesame seeds.

Moreover, in North Africa, Sumac is often rubbed on meats, chicken, or fish to add a tart, lemony taste. And it is added to marinades, and it can be added to egg dishes and salads to enhance their taste and flavor (Batiha *et al*., 2022).

Sumac appeared in cookbooks in Western Europe during medieval times, from the thirteenth to fifteenth centuries, in a dish called sumāqiyya, a stew made from Sumac.

2.6.2. Uses of Sumac in the food industry

There is increasing interest in using plant extracts by the food industry as natural antioxidants, preservatives, and fortifying agents. Aqueous extracts of *Rhus coriaria* have a potent antibacterial and antioxidant effect against pathogenic food-borne bacteria, allowing it to be used as an effective and natural preservative in food manufacturing to control lipid oxidation and microbial growth in food to increase products' shelf life maintaining its quality (Aliakbarlu *et al*., 2014).

In a study conducted to evaluate the antimicrobial effects of Sumac extract on spoilage and pathogenic bacteria in minced meat, it was reported that the ethanol extract of Sumac is significantly effective in reducing the total microbial and *Salmonella* count in minced meat for one week (Radmehr and Abdolrahimzade, 2009).

Similarly, Gulmez *et al*. conducted a comparative study that evaluated the surface decontamination and shelf-life activity of Sumac extracts used at a concentration of 8% (wt. /vol.), distilled water, and lactic acid on raw broiler meat, to improve the bacteriological quality and refrigerated shelf life of broiler chicken meat. The

antimicrobial effectiveness of Sumac extract against contaminating bacteria (psychrotrophic, mesophilic aerobes, Enterobacteriaceae, coliforms, and fecal coliforms) was comparable to that of lactic acid and higher than that of distilled water. Thus, Sumac could act as a surface decontaminant alternative to synthetic and chemical antimicrobials in the poultry industry, as it is also a natural, cheaper, and safer option. In addition, Sumac-treated wings showed no sign of color fading or spoliation of the meat. In contrast, both distilled water-treated wings and lactic acid-treated wings developed an unpleasant color. This gives a positive score for the use of Sumac in poultry processing (Gulmez *et al*., 2006).

Moreover, the Sumac extract had used in the sausage industry to enhance its total quality by preventing lipid oxidation, as it is more effective than BHT in enhancing the quality parameters of the fermented sausage. (Bozkurt, 2006). Also, the Sumac extract was effective in stabilizing peanut oil compared with BHA, in which the antioxidant efficiency lasted for about four weeks (Ozcan, 2003). Another study showed that the fortification of yogurt samples with aqueous extracts of Sumac leaf resulted in a significant increase in the total phenolic compounds and antioxidant activity in comparison with plain yogurt (Perna *et al*., 2018).

Natural alternatives for additives have recently grown globally. Food colorants are applied in several areas of the food industry and are an important ingredient in many products (Dabas, 2016), such as beverages, packaged foods, dairy products, frozen foods, condiments, dressings, functional foods, and pet foods.

Sumac is used as a colorant, as the anthocyanins, the main phenolic compound in Sumac, are well-reported and used pigments that vary in hue from orange, red, blue, or purple in color, and these pigment compounds are stable colorants even if mixed with water. The red-like pigmentation was found in wine and Sumac and identified as hydroxyphenyl pyranoanthocyanins (Dabas, 2016).

2.6.3. Traditional therapeutic uses of Sumac

Rhus coriaria has been used in Middle Eastern and South Asian countries, for thousands of years, as a traditional medicine to treat many ailments. The medicinal value of Sumac was first described nearly 2000 years ago by the Greek physician and

botanist Pedanius Dioscorides (40–90 AD) in his writings "De Materia Medica", especially as an anti-flatulent and diuretic (Abu-Reidah *et al*., 2014).

Sumac has been used traditionally to treat several illnesses that include diarrhea, liver disease, urinary system disorders, ulcers, animal bite pain, and hemorrhoids (Sezik *et al*., 2001; Said *et al*., 2002; Lev, 2002; Shabbir, 2012). In addition, powdered Sumac fruits were also used to stimulate perspiration and reduce cholesterol (Lev and Amar, 2002). Recently, studies predicted that Sumac phytochemicals could inhibit COVID-19 (Sherif *et al*., 2021; Korkmaz, 2021).

Different parts of the plant have been used in traditional medicine, with powdered bark has been used as an effective teeth-cleaning agent, and the bark infusion has been used to treat viral eye infections (Shabbir, 2012; Batiha *et al*., 2022).

2.7. General Composition and Minerals and Vitamins Contents of *Rhus coriaria*

Rhus coriaria is considered a rich and valuable dietary source of nutrients which include unsaturated fatty acids, vitamins, and minerals.

2.7.1. General composition

Studies have shown estimates of the general composition of fresh and dried Sumac fruit. Fresh Sumac to be 10.6% moisture, 2.6% protein content, 14.6% fiber content, 7.4% fat, 1.8% ash, and water-soluble extract 63.8% (Ozcan and Haciseferogullari, 2004). And found in dried Sumac 2.43% moisture, 4.69% protein, 18.74% fat, and 2.93% ash (Raodah *et al*., 2014). Also, a calorimetric calculation showed that 100 grams of Sumac fruit contain 147.8 kcal (Ozcan and Haciseferogullari, 2004).

2.7.2. Mineral's composition

The mineral composition of Sumac fruits showed that potassium, calcium, magnesium, and phosphorus are the predominant elements in the Sumac fruit, followed by aluminum, iron, sodium, boron, and Zinc (Ozcan and Haciseferogullari, 2004).

2.7.3. Vitamins composition

Although, studies on the vitamin composition of *Rhus coriaria* are still lacking. A comparative study between Syrian Sumac and Chinese Sumac revealed that Sumac fruit is rich in pyridoxine, ascorbic acid, thiamine, and riboflavin. Other vitamins reported include cyanocobalamin, nicotinamide, and biotin (Sakhr and El Khatib, 2020).

2.8. Phytochemicals constituents of *Rhus coriaria* L.

Several studies have been performed to identify the major phytochemicals of *Rhus coriaria* and its bioactive compounds as well as fatty acid composition. More than 250 bioactive compounds have been detected from various extracts of the Sumac plant's fruit, leaf, and stem samples, and these include organic acids, phenolic acids, phenolic compounds conjugated with malic acid derivatives, flavonoids, isoflavonoids, hydrolysable tannins, anthocyanins, terpenoids, and other compounds such as butein, iridoid, and coumarin derivatives. Some of the main phytochemicals reported in the plant of *Rhus coriaria* are summarized in **Table 2.1.**

Table 2.1: Summary ot the main phytochemicals present in *Rhus coriaria* L.

Classes of compounds	Examples of important Bioactive compounds	%
Taninnis	Gallotannins and derivatives, methyl gallate, digallic acid, tri-gallic acid, ellagic acid.	36%
Flavonoids	Quercetin, isoquercitrin, quercitrin, rutin, keampferol, myricetin, apigenin, isorhamnetin, isovitexin, rhamnetin, ampelopsin, glycitein-O-glucoside, oxoglycyrrhetinic acid, amenthoflavone, agathisflavone, hinokiflavone and sumaflavone	30%
Conjugated phenolics	Galloyl-hexose-malic acid, digalloyl-hexose malic acid, keampferol-hexose malic acid, quercetin-hexose malic acid, Isorhamnetin hexose malic acid	12%
Anthocyanins	Cyanidin, peonidin, pelargonidin, petunidin, coumarates, delphinidin, myrtillin, crysanthemin	4%
Phenolic acids	Protocatechuic acid, syringic acid, coumaryl-hexoside, caffeoylquinic acid, p-benzoic acid, vanilic acid	4%
Organic acids	Malic acid, citric acid, tartaric acid, linoleic acid, oleic acid, linolenic acid, palmitic acid, stearic acid	4%
Terpenoids	Betunolic acid, alpha-tocopherol, tocopherol mannoside.	3%
Essential oils	Beta caryophyllene, cembrene, limonene, nonanal and (Z)-2-decenal	3%
Steroids	Beta-sitosterol	1%
Others	Butein, Iridoid and coumarin derivatives	3%

Adopted from: Kosar *et al*., 2007; Kossah *et al*., 2009; Abu-Reidah *et al*., 2015; Ardalani *et al*., 2016.

In 2015, Abu-Reidah *et al*. investigated the phytochemical composition of the extract of Sumac fruits cultivated in Palestine, using HPLC–DAD–ESI-MS/MS, 211 phytoconstituents have been identified of which 180 were characterized for the first time in *Rhus coriaria* fruits, including tannins, (iso) flavonoids, terpenoids, anthocyanins, phenolic acids, conjugated phenolic acids, organic acids, coumarins, xanthones, terpenoids, steroids, essential oils, and many more (Abu-Reidah *et al*., 2015). The distribution proportion of the 211 different chemical constituents of *Rhus coriaria* in sub-classes is shown in **Figure 2.2**.

In addition, a qualitative analysis was performed in Iran for the phenolic composition of Sumac using the HPLC-MS method. And a total of 191 compounds were identified in Sumac fruit including; 78 hydrolysable tannins, 59 flavonoids such as Apigenin, nine anthocyanins such as Cyanidin, two isoflavonoids, two terpenoids, one diterpene, 38 other unidentified compounds (Ardalani *et al*., 2016).

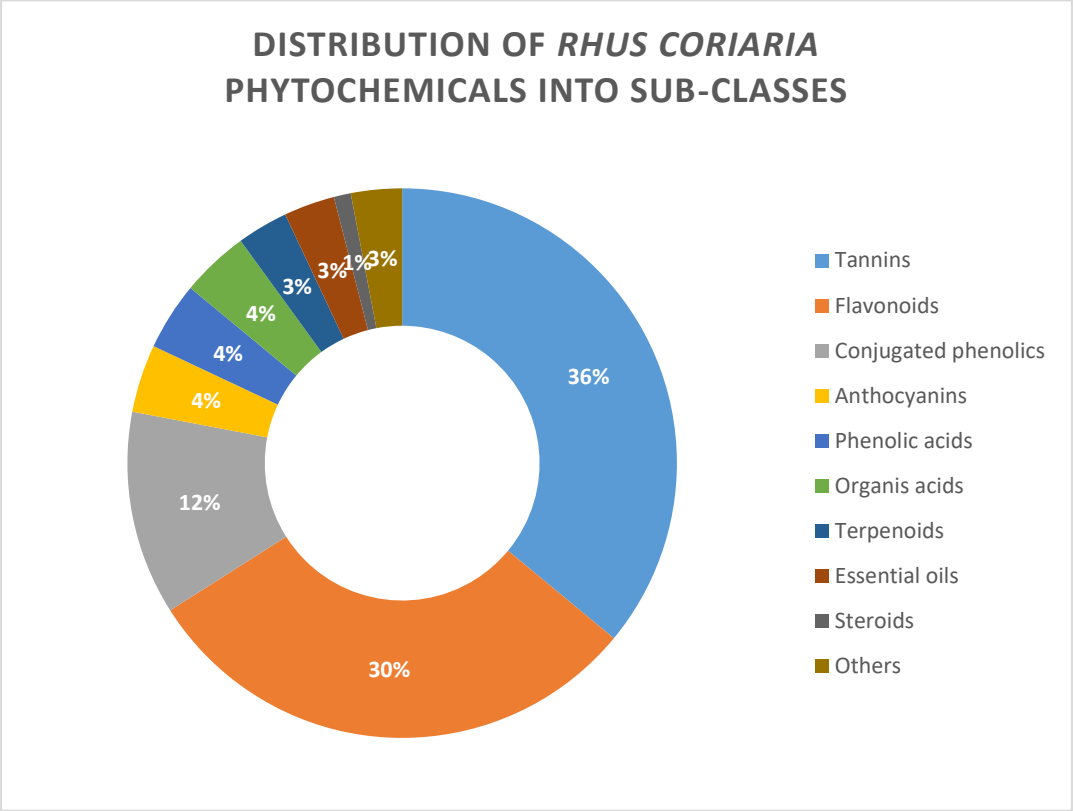

Figure 2.2: The distribution of *Rhus coriaria* phytochemicals into sub-classes.

2.8.1. Phenolic compounds in Sumac

Hydrolyzable tannins make up the highest percentage of the Sumac fruits, constituting nearly 20% of the fruit's mass, followed by flavonoids, confirming the fruit's antioxidant potential and explaining the old use of Sumac to tan leather (Ardalani *et al*., 2016).

Gallotannins, which are hydrolyzable tannins, are the most abundant tannin compounds found in the *Rhus* genus, mostly in *Rhus coriaria* specie, which is an abundant source of tannins with different isomers and conjugations. In *Rhus coriaria*, six gallotannins have been identified these were penta, hexa, hepta, octa, nona, and decagalloyl-glucoside (Abu-Reidah *et al*., 2014; Sakhr and El Khatib, 2020; Romeo *et al*., 2015).

It is worth noting that the tannins are the compounds responsible for the astringent taste of Sumac, while the sourness of Sumac is due to the presence of organic acids, such as malic, citric, and tartaric acids (Abu-Reidah *et al*., 2014).

Among the flavonoids, the principally identified flavonoids in Sumac are quercetin 3-O-galactoside, kaempferol 3-O-glucoside, quercetin, and myricetin 3-O-hexoside. Also, Flavonoid dimers like amentoflavone, agathisflavone, hinokiflavone, and sumaflavone have also been identified in the leaves and fruits of Sumac (Abu-Reidah *et al*., 2015; Romeo *et al*., 2015).

Moreover, the presence of anthocyanins derivatives: Delphidin-3-glucoside, Cyanidin 3-(200-galloyl) galactoside, Cyanidin-3-glucoside, 7-methyl--cyanidin-3-(200-galloyl) galactoside, 7-methyl-cyanidin-3-galactoside have also been reported from the fruits of Sumac (Abu-Reidah *et al*., 2015; Romeo *et al*., 2015). The structures of some selected polyphenolic compounds in *Rhus coriaria* L are shown in **Figure 2.3.**

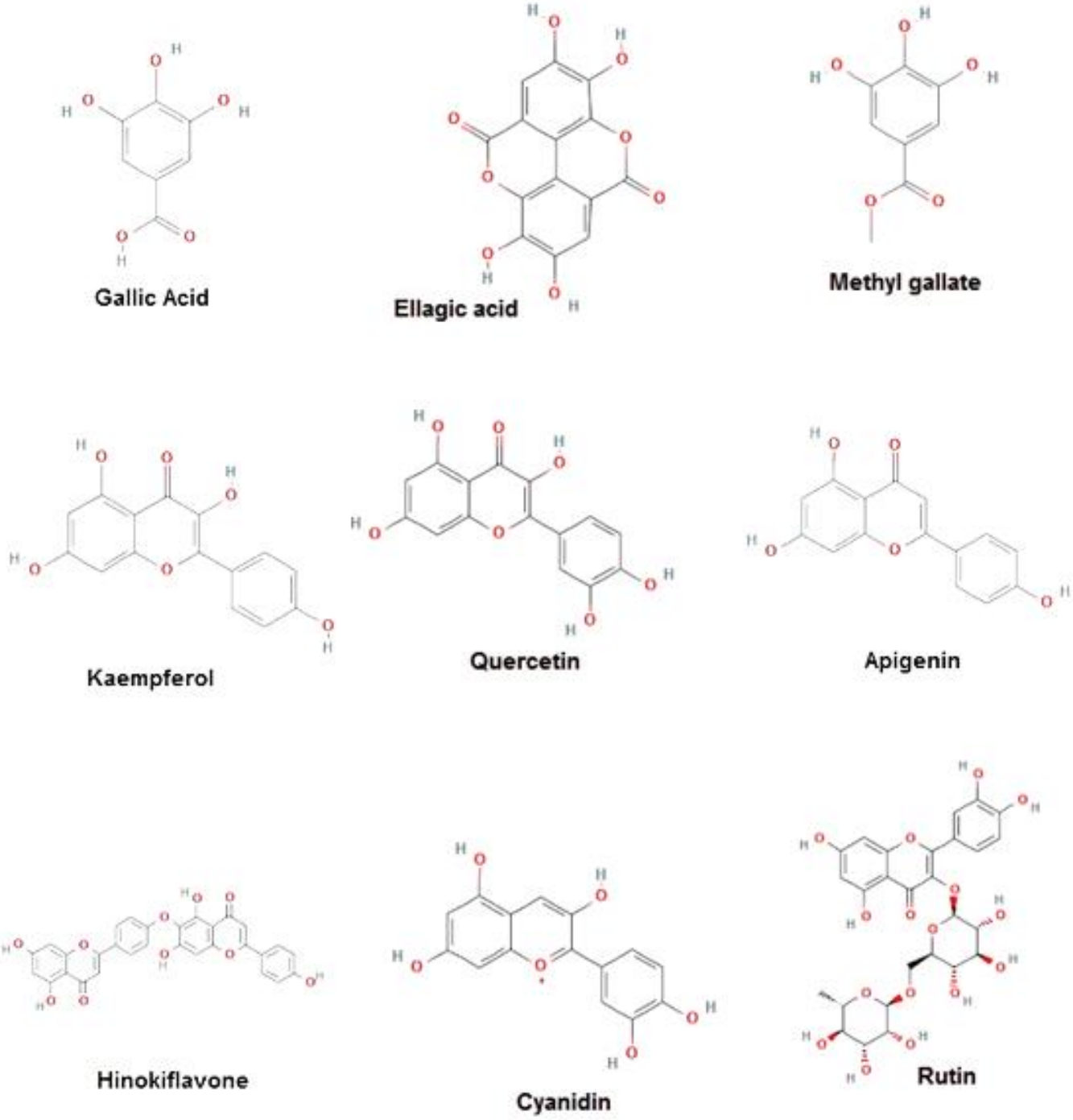

Figure 2.3: The structure of selected polyphenolic compounds in *Rhus coriaria* L.

However, several studies showed that the properties of Sumac extracts depend both on the polyphenols' content, which has a role in reducing lipid absorption due to the high resin-binding capacities and greater anti-inflammatory properties and on the tannins, which contribute to the antioxidant properties due to their action against the xanthine oxidase, which is involved in cholesterol metabolism. Among the factors that could influence the composition of Sumac extracts are the climatic conditions of the place where the Sumac grows, and the harvesting period (Calabrò *et al*., 2023). The study of volatile compounds in Sumac from different regions showed different amounts of monoterpene hydrocarbons and oxygenated monoterpenes due to different soil compositions and climatic conditions (Giovanelli *et a*l., 2017).

Other factors that could influence the composition of the Sumac extracts are the extraction solvent needed to isolate the polyphenols, wherein a study indicated that the methanolic extract from fruit showed the highest total phenolics content (151.71 mg g^{-1}), followed by ethyl acetate (65.31 mg g^{-1}) and aqueous extracts (6.10 mg g^{-1}) (Raodah *et al*., 2014).

A similar evaluation was made in Baghdad on aqueous, methanolic, and ethanolic extracts, and it was also found that the methanolic extracts contained a higher amount of phenolics and flavonoids than ethanolic and aqueous extracts. Thus, making it the best solvent for the extraction of phenolics from Sumac (Al-Muwaly, *et al*., 2013).

2.8.2. Essential oils of Sumac

The analysis of essential oils from Sumac fruits reveals that Terpene hydrocarbons, specifically β-caryophyllene and α-pinene, are the predominant chemical classes in *Rhus coriaria* extracts, followed by diterpenes (Reidel, 2017). Despite being considered an essential oil-poor plant, recent studies, particularly using microwave-assisted extraction, have significantly increased the yield of Sumac oil to approximately 13.5% (Gharaei, 2013).

In contrast to non-volatile constituents, the focus on the volatile composition *of Rhus coriaria* has been relatively limited. An analysis conducted in 2018 provided a comprehensive overview of the volatile profile of Sumac fruit sourced from Egypt, Jordan, and Palestine. This study emphasized variations in volatile components depending on the region of harvest. Fresh fruit primarily exhibited sesquiterpene

hydrocarbons, while roasted fruits showcased a prevalence of furan/aldehydes. Variation in volatile profiles was observed across regions, with Egyptian Sumac showing greater diversity in tea or roasted profiles compared to Palestinian and Jordanian Sumac (Farag *et al*., 2018).

Additionally, a separate study in Turkey identified malic acid in the volatile fraction as the cause of the sour flavor in *Rhus coriaria* fruit. Furthermore, chemicals such as β-caryophyllene, cembrene, and caryophyllene oxide were found to contribute to the overall flavor profile (Bahar and Altuğ, 2009).

2.8.3. Fatty acid

Kossah *et al.* using Gas Chromatography revealed that the fatty acids compositions of the Syrian Sumac were mostly unsaturated with 69.28% of the total fatty acids, which consisted mainly of oleic followed by linoleic and linolenic acids. Regarding saturated fatty acids, the predominant fatty acid were palmitic acids (27.41%) (Kossah *et al*., 2009).

These are comparable with those reported by Dogan and Akgül on Sumac growing in Turkey, as it was reported that the major fatty acids in the Sumac were oleic (C 18:1), linoleic (C 18:2), and palmitic (C 16:0) acids. The oleic acid contents ranged from 34.00 to 40.35 % while the linoleic and linolenic acid contents ranged from 33.31 to 35.83 % and 1.53 to 2.99 %, respectively. As for the palmitic acid content in the study, it ranged between 20.75 % and 25.60 % (Dogan and Akgül, 2005).

Sumac also has been found to contain fatty acids that contributed minimally to the total fatty acids such as Myristic acid, Palmitoleic acid, and Stearic acid.

2.9. Pharmacological and Biological Properties of *Rhus coriaria* L

A range of pharmacological and biological activities have been linked to different parts of *Rhus coriaria*. The bioactive compounds in Sumac are suggested to demonstrate a large spectrum of actions, with antibacterial, antifungal, antiviral, anti-inflammatory, antioxidant, antiemetic, antidiarrheal, hypoglycemic, and cardioprotective effects, thanks to the properties of its phytochemicals (Abu-Reidah *et al*., 2014;Sakhr and El Khatib, 2020; Alsamri, 2021).

2.9.1. Antioxidant potentials of Sumac

Sumac has gained a reputation as a functional food plant because of its antioxidant activity, which is due to the presence of phenolic compounds in the fruit. There are extensive reports on the antioxidant capacity of various extracts and chromatographic fractions derived from Sumac fruits. For instance, Mahdavi *et al*. estimated the antioxidant capacities of ripe Sumac fruits using DPPH assays, ethanolic Sumac extract showed a high antioxidant effect, higher than BHT in all of the examined concentrations (Mahdavi *et al.*, 2018). Also, a study of the antioxidant potential ability of Sumac aqueous extract among other spices using DPPH and reducing power tests revealed that the aqueous extracts of Sumac exhibited the highest antioxidant capacities among the other studied extracts (Aliakbarlu *et al*., 2014). Further, Shafiei *et al*. revealed the antioxidant, free radical scavenging, and lipid peroxidation inhibitory capacity of the methanolic extracts of the Sumac fruits. And also indicated that the plant extract possesses cardioprotective and hepatoprotective activities and the potential for chronic disease prevention such as atherosclerosis, which would be beneficial in hypercholesterolemic conditions (Shafiei *et al*., 2011).

Taskin *et al.* conducted another recent study, evaluating Sumac leaf methanolic extract through various antioxidant tests, including DPPH, FRAP, CUPRAC, and ABTS. The results consistently indicated strong antioxidant and scavenging activity in Sumac leaf extract (Taskin *et al*., 2020).

In the context of skin health, where oxidative stress is often induced by exposure to ultraviolet (UV) radiation, *Rhus coriaria* has demonstrated significant photoprotective properties. UV-A and UV-B radiation are known to be harmful to the skin, with UV-A having the ability to deeply penetrate dermal layers. Studies on cutaneous microvascular endothelial cells (HMEC-1), as a model, have shown that the macerated ethanol extract of *Rhus coriaria* fruit provides photoprotection against UV-A-induced damage. The extract not only inhibits the creation of DNA damages in cells exposed to medium UV-A dosages but also reduces the generation of ROS induced by UV-A. However, the molecular mechanisms underlying the genoprotective and antioxidant properties of the extract require further investigation (Nozza *et al*., 2020).

In the context of oxidative stress induced by hydrogen peroxide, *Rhus coriaria* extract has demonstrated potent antioxidative activity on human myoblasts and zebrafish

embryos. This activity is attributed to the extract's ability to inhibit oxidative stress through catalase and superoxide dismutase 2, potentially delaying the progression of skeletal muscle atrophy (Najjar *et al*., 2017).

Furthermore, due to the antioxidant potency of Sumac, it could be added as a complementary natural antioxidant and preservative to food, in a study to determine the antioxidant activity of Sumac extracts at various concentrations on peanut oil stored at 65°C, compared to a reference commercial synthetic antioxidant compound, such as BHA. Sumac extract at concentrations 1.0%, 3.0%, and 5.0% (wt./vol.) inhibited the formation of hydroperoxide and increase oxidative stability in peanut oil, such as BHA, but the antioxidant effects of the extracts decreased significantly after four weeks of storage (Ozan, 2003). Another study evaluated the oxidative stability of corn oil under accelerated oxidation at 60 °C for 6 weeks, Sumac extract with IC_{50} of 29.89 µg/mL exhibited strong antioxidant activity in DPPH radical scavenging assay. In addition, Sumac significantly inhibited the formation of thiobarbituric acid reactive substances. These findings imply that Sumac could be used in the food industry for commercial purposes in the retardation of oil oxidation (Baştürk *et al*., 2018).

Another study reported that the antioxidant capacity of the Sumac methanolic fruit extract for lipid peroxidation inhibition was estimated as 1200 µg/mL in the Fe^{-2} ascorbate system. As well, Sumac exhibited an uncompetitive strong inhibition activity on xanthine oxidase with an IC_{50} value of 173 µg/mL, which explains its serum cholesterol-reducing effects (Candan and Sökmen, 2004).

Studies have attributed the antioxidant capacity of Sumac to the constituent polyphenolic compounds, especially, gallic acid and its derivatives. Gallic acid and other polyphenols are strong antioxidant compounds that are capable of donating hydrogen radicals to the free radicals formed during oxidation becoming radicals themselves that are stabilized by the resonance delocalization of the electron within the aromatic ring Gabr *et al*. revealed that several polyphenols isolated from the *Rhus coriaria* fruit samples exhibited strong free radical scavenging activities *in vitro*, using β-carotene-linoleic acid and DPPH methods as compared to those of glycosides, alkaloids, and terpenoids respectively (Gabr *et al*., 2014).

2.9.2. Antibacterial potential of Sumac

Recently, there is a huge increase in bacterial resistance to many antibiotics, which poses a serious threat to humans. Thus, Interest in medicinal plants has increased to explore the antimicrobial effects of natural compounds and to identify new antibacterial agents as a novel approach to limit the phenomenon of antibiotic resistance.

On this basis, Adwan *et al*. investigated the antibacterial activity of water, ethanolic and methanolic extracts of Sumac against five clinical species of bacteria, the results indicated the existence of antimicrobial activity in the crude extracts of Sumac seeds. Water extract was more active against gram-positive than gram-negative bacteria, while ethanolic and methanolic extract showed a broad spectrum of growth inhibition activity on gram-positive and gram-negative bacteria (Adwan *et al*., 2015). Similarly, another study reported that Sumac ethanolic extract showed strong antibacterial activity against gram-positive and gram-negative bacteria, with MIC < 0.78% (Mahdavi *et al.*, 2018).

In addition, Ali-Shtayeh *et al*. compared the antimicrobial activity of *Rhus coriaria* among the 50 Palestinian medicinal plants against acne vulgaris, the study revealed that the ethanolic extract of *Rhus coriaria* showed an inhibitory effect and found to be between the main active plant extracts against most bacterial strains tested including *P. acnes*, and gram-negative strains of aerobic bacteria (Ali-Shtayeh *et al.*, 2013). Further, Raodah *et al*. studied the *Rhus coriaria* extracts antimicrobial activity against three gram-negative and three gram-positive strains. The *Bacillus subtilis* was the most sensitive gram-positive with MIC of 0.5 mg/ml, while higher concentrations of Sumac were needed against gram-negative bacteria with extracts concentrations ranging from 10–20 mg/ml (Raodah *et al*., 2014). Also, a recent study revealed that the hydrophilic extract of Sumac had effective antimicrobial activity against a set of microbes especially *S. aureus, P. aeruginosa*, and *S. aureus* (MRSA) *in vitro*, and could play a good potential role in accelerating wound healing (Gabr and Alghadir, 2019).

These findings support the traditional use of *Rhus coriaria* as a disinfectant and deserve further studies toward the isolation of novel antibiotic molecules that could be employed to treat microbial infections.

2.9.3. Anti-cancer potentials of Sumac

Studies have reported promising effects of Sumac extracts on apoptosis and cancers. Mirian *et al*. studied the cytotoxicity properties of methanol extract of *Rhus coriaria's* oleo gum resin on HUVEC and retinoblastoma cell line and reported a dose-dependent anti-angiogenic effect. Also, Abdallah *et al.* indicated that Sumac has growth-inhibitory impacts on cervical cancer cells in a time- and concentration-dependent manner, which can be utilized as a therapeutic drug agent for uterus cervix cancer (Abdallah *et al.*, 2019).

Similarly, the ethanolic extract of dried Sumac fruits had a cytotoxic effect against breast cancer cells that depended on the promotion of cell growth inhibition, cell cycle arrest, cellular senescence, apoptosis, and autophagic cell death. The same group lately reported that ethanolic extracts of Sumac also possessed strong antitumor activity against human colorectal cancer cells, due to the stimulation of proteolysis as well as the induction of autophagic and apoptotic cell death (El Hasasna *et al*.; 2015).

2.9.4. Anti-diabetic and anti dyslipidemic activities of Sumac

In a study that investigated the in vivo healing and protective effects of lyophilized extract Sumac against streptozotocin (STZ)-induced diabetic complications, the Sumac extract decreased the levels of blood glucose in diabetic rat groups treated orally with the extract for three weeks, by an average value of 31%. The authors further reported that the Sumac extract caused a significant reduction in the serum level of triglycerides, total cholesterol, LDL, and the level of HbA1c and alpha-glucosidase activity while it significantly reduced serum insulin levels in the experimental rats (Dogan and Celik, 2016).

Another study revealed that the administration of Sumac seed extract in two doses of 200 and 300 mg/kg orally for 28 days decreased the level of glucose and cholesterol significantly in diabetic mice (Ahangarpour *et al*., 2017).

Moreover, the extracts from Sumac fruits exhibited antidiabetic potential through the inhibition of alpha-amylase. As the methanol extract showed 48.3% inhibition of α-amylase, while the ethyl acetate extract inhibited the α-amylase by 87%. It was proposed that tannins and flavonoids especially quercetin could be responsible for the

blood glucose lowering effects by blocking the absorption of glucose in the intestine by inhibiting the alpha-amylase enzyme (Giancarlo *et al*., 2006).

Noteworthy, clinical studies have also demonstrated the hypoglycemic effect of Sumac in diabetic patients. Where three grams of *Rhus coriaria* powder were supplemented daily along with aerobics and walking activity in a type II diabetic women's diet, resulted in increased total antioxidant capacity and significantly decreased insulin resistance index and blood glucose levels. Also, the anthropometric measures (weight and body mass index) decreased significantly (Azali, 2017).

Furthermore, a daily intake of 6 g of Sumac powder decreased fasting serum insulin level and insulin resistance in patients with type II diabetes (Ardakani *et al*., 2016). Also, in a double-blind randomized controlled clinical trial to determine the effects of Sumac on type II diabetes by examining serum glycemic status, apo B, apoA-I, and total antioxidant capacity in type II diabetic patients consuming a powder of Sumac (3.0 g, daily for three months), results showed a significant decrease in the levels of serum glucose, HbA1c, apoB, and apoA-I, and an increase in the total antioxidant capacity (Shidfar *et al*., 2014).

2.9.5. Neuroprotective, cardioprotective, anti-ischemic, and anti-coagulation potentials of Sumac

Atherosclerosis is the main underlying cause of cardiovascular disease, including myocardial infarction, heart failure, stroke, coronary heart disease, carotid artery disease, renal artery stenosis, and peripheral artery disease. Collectively, comprise the number one cause of death globally (Wang *et al*., 2018).

Many natural products and herbal medicine have been taken into consideration in managing cardiovascular risk factors. *Rhus coriaria* is one of these natural plants, due to its bioactive compounds that can improve cardiovascular health (Alsamri, 2021).

Indeed, Khalilpour *et al*. assessed the neuroprotective and anti-neuroinflammatory properties of ethanolic Sumac fruit extract against ischemic optic neuropathy in mice, the results providing conclusive evidence for the neuroprotective activity of the ethanol *Rhus coriaria*, and identifying linoleic acid as one of the main constituents responsible for this effect (Khalilpour *et al*., 2018).

Another study revealed that methanolic extract derived from Sumac leaf samples exhibited cardiovascular protective activity in isolated rabbit hearts. The authors reported that the leaf samples of Sumac were able to induce normalization of coronary perfusion pressure, reduction of left ventricular contracture during ischemia, improvement of the maximum rate of rise and fall of left ventricular pressure at reperfusion in male rabbits in a dose-dependent manner.

Further, the cardiovascular protective effect of Sumac is attributed to COX pathway activation, TNF-inhibition, eNOS activation, and free radical and ROS scavenging (Beretta *et al*., 2009).

Moreover, in patients with dyslipidemia, a study reported that the endothelial vasodilator function as indicated by the flow-mediated dilation significantly improved after consumption of 0.5 g of Sumac fruits on a daily basis for one month (Asgary *et al*., 2018).

A study isolated 6-Pentadecylsalicylic acid from *Rhus semialata*, Chinese Sumac another species of *Rhus* genus, this extract exhibited antithrombin activity at 50 μg/mL in the amidolytic method, and the coagulation test, which measured the thrombin-fibrinogen interaction, yielded prolonged coagulation time in a dose-dependent manner. This indicates that *Rhus coriaria* Sumac could be also a protective agent for coagulopathy or for decreasing the tendency of thrombosis (Kuo *et al*., 1991).

Chapter Three: Methodology

3. Methodology

3.1 Plant Collection

Sumac (*Rhus coriaria* L.) fruits were obtained from three different sources: The first and the second sets, represent wild sumac plants indigenous to the region, were collected between March and April 2022, from two locations in the Hebron area, Palestine. The first collection site, Bair Al-Mahjar, is situated approximately five kilometers northwest of Hebron's city center. The second collection site, Ain der-Baha, is located about three Kilometers from Hebron city center to the west. The Sumac source collected from Bair Al-Mahjar will be referred to as 'Palestinian 1' in the subsequent sections of this study. Similarly, the sumac source gathered from Ain der-Baha will be denoted as 'Palestinian 2'. The third set of Sumac fruits, presenting cultivated plant, was imported from Turkey and purchased from a local market in the city of Hebron, Palestine.

Figure 3.1: Sumac fruits collection from Hebron (a) Sumac Fruit, (b) Sumac plant.

3.2 Extract Preparation

Twenty grams of ripe red Sumac fruits from each sample were shade-dried at room temperature for one week. All fresh and dried samples were then stored in dark, sealed bags at room temperature until needed for extraction.

Extraction Procedure:

A total of eighteen extracts were prepared, with six extract samples from each of the three sources. Two different extraction methods were employed: reflux and room temperature (RT) shaking. **Figure 3.2** shows the scheme for the preparation of extracts from plant samples.

In both methods, the whole fruits with shell and seeds were ground into fine powders using an electric grinder. Subsequently, five grams of the resulting powder were extracted with 50 ml of solvent. Two different concentrations of methanol were used for extraction: absolute methanol (100% MeOH) and a mixture of methanol and water (80:20 methanol: water, 80% MeOH).

The reflux extraction was conducted for fresh Sumac fruits, whereas the RT extraction was performed for both dried and fresh Sumac fruits.

In RT extraction, 5g of each sample was extracted with 50 ml of each solvent (100% MeOH and 80% MeOH). This mixture was placed in a shaking incubator and maintained at 25°C for 24 hours. Whereas for reflux extraction samples were refluxed for 24 hours under constant heat that brought the mixture to boil

Following extraction, the extracts were separated from any remaining residues by filtering through Whatman No. 1 filter paper. Subsequently, they were stored in a freezer at -20°C until use**.**

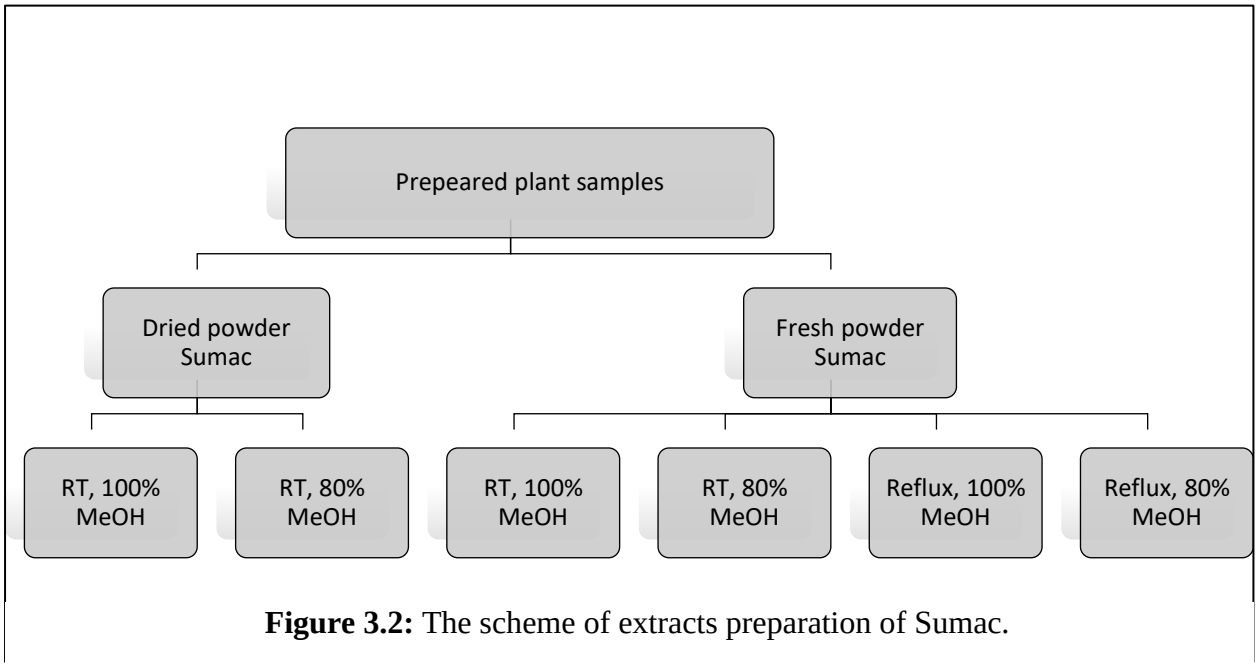

Figure 3.2: The scheme of extracts preparation of Sumac.

3.3 Screening of Antibacterial Activity of *Rhus coriaria* L Extracts

The *in vitro* antibacterial activities of the Sumac extracts were evaluated against gram-positive Methicillin-resistant *Staphylococcus aureus* (MRSA), and gram-negative Extended Spectrum Beta-Lactamase (ESBL). Muller Hinton agar plates were purchased from reliable commercial vendors, and antibiotic discs: Meropenem disc (Biolab Zrt, 10 mcg, Budapest) and Co-Trimoxazole (Sulpha/Trimethoprim) disc (Himedia, 1.25/23.75 mcg, India).

3.3.1 Microbial Strains Collection

Two bacterial strains, MRSA and ESBL, were isolated from blood samples collected at Al-Ahli Hospital laboratory in Hebron, Palestine. These strains were cultured on nutrient agar and incubated at 37 °C for 24 hours. Cultured plates containing these bacterial strains were then refrigerated at 2–4 °C for future use.

3.3.2 Preparation of Sumac Extract

The Sumac fruit extract samples for the antibacterial test were prepared as described previously in the Extract Preparation section (Section 3.2).

3.3.3 Bacterial Suspension Preparation

Bacterial suspensions for each strain were prepared by suspending bacterial colonies in a sterile NaCl solution using a sterile cotton swab until the broth reached a turbidity of 0.5 McFarland (approximately 1.5×108 CFU). Turbidity was standardized by visually comparing the microbial suspension to a 0.5 McFarland standard.

3.3.4 Susceptibility Testing

The sensitivity of bacterial species to Sumac extracts was assessed using the disk diffusion method (Kirby–Bauer method) on Muller Hinton agar plates, following the guidelines set by the Clinical and Laboratory Standards Institute (2012).

In this procedure, bacteria were evenly spread on the surface of the Muller Hinton agar plate using a sterile swab from the adjusted suspension. This streaking process was repeated three times, with the plate rotated each time to ensure even bacterial distribution.

After a few minutes, four discs were spread on the surface of the media in each plate in addition to the reference antibiotic disc (positive control). One disc for the negative

control (20 µl of methanol) and 20 µl of Sumac extracts was added to the remaining discs.

The testing was conducted in triplicate, and all plates were then incubated at 37°C for 24 hours. Following incubation, the plates were examined for bacterial growth inhibition, and the diameter of the inhibition zone was measured to the nearest millimeter. The results were documented.

As positive controls, Co-Trimoxazole was used for MRSA, and Meropenem 10 mcg was used for ESBL.

3.4 Evaluation of the Antioxidant Activity of *Rhus coriaria* L Extracts

The antioxidant and scavenging activity of *Rhus coriaria* L extracts were determined using 2, 2'-diphenyl-1-picrylhydrazyl (DPPH) and 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulphonate ($ABTS^{+}$) assays, they both are spectrophotometric techniques based on quenching of stable-colored radicals (ABTS•+ or DPPH). Both show the radical scavenging ability of antioxidants even when present in complex biological mixtures as plant extracts.

3.4.1 Radical Scavenging Activity Using 2, 2'-diphenyl-1-picrylhydrazyl (DPPH) Assay

Electron's donation ability of *Rhus coriaria* L essential oils was measured from the bleaching of purple-colored methanol solution of stable radical DPPH using a spectrophotometric assay. After the incubation period, the absorbance was measured at 517nm. The ability of methanolic extracts of Sumac fruits to donate electrons to the stable and violet-colored free radical DPPH to yield a non-radical compound was measured using a spectrophotometer. Therefore, the number of antioxidants in Sumac extracts that reacted with DPPH is proportional to the decrease in absorption.

3.4.1.1 Chemicals

2, 2–Diphenyl-2-picrylhydrazyl (DPPH) was purchased from Sigma (D9132, Sigma-Aldrich, Germany); methanol and all other chemicals and reagents were of analytical grade.

3.4.1.2 Apparatus

The UV/Visible Scanning Spectrophotometer used for reading the absorbance was the UV-Vis spectrophotometer was Jenway 7205 (Cole-Parmer Ltd, UK).

3.4.1.3 Preparation of Sumac Extract

The Sumac fruit extract samples for the antioxidants test were prepared as described previously in Extract Preparation section (Section 3.2).

3.4.1.4 DPPH• Assay Protocol

To assess the effect of Sumac extracts on DPPH•, according to (Qawasmeh, *et al*., 2012) with minor modification the following steps were performed:

1. A DPPH• stock solution was prepared by dissolving 10 mg of DPPH• in 25 mL of 80% v/v methanol.

2. The absorbance of the stock solution was measured at a wavelength of 517 nm. The solution was then diluted with 80% v/v methanol until the absorbance reached approximately 0.8.

3. In plastic cuvettes, 30 µL of diluted Sumac extracts were added to 2 mL of DPPH solution (with an absorbance of 0.722). The cuvettes were mixed using a vortex and incubated in the dark at room temperature for 1 hour.

4. After the incubation period, the absorbance was measured at 517 nm using a UV/Visible spectrophotometer.

5. The blank consisted of methanol, and a control was prepared using the solvent along with DPPH reagent in the same amount to account for any inherent solvent activity.

6. The experiments were conducted in triplicates.

7. The ability to scavenge the DPPH radical was calculated using the formula: (Baliyan *et al*., 2022)

$$\%\text{DPPH radical scavenging activity} = [(A_{control} - A_{sample}) / A_{control}] \times 100\%$$

Where,

A_{sample}: Sample absorbance and $A_{control}$: Control absorbance

3.4.2 Radical Scavenging Activity Using 2, 2′-azinobis-(3-ethylbenzothiazoline-6-sulphonate (ABTS•+)

In the $ABTS^{\bullet+}$ radical scavenging assay, the dark blue-green color of the ABTS•+ radical cation in the presence of antioxidants in the extracts reduced to colorless ABTS which can be measured spectrophotometrically (decrease in absorption).

3.4.2.1 Chemicals

2, 2-Azino-bis (ethylbenzothiazoline-6-sulfonic acid) diammonium salt (ABTS) was purchased from Sigma (A188, Sigma-Aldrich, Germany); potassium persulfate, distilled water, methanol, and all other chemicals and reagents were of analytical grade**.**

3.4.2.2 Apparatus

The UV/Visible Scanning Spectrophotometer used for reading the absorbance was the UV-Vis spectrophotometer was Jenway 7205 (Cole-Parmer Ltd, UK).

3.4.2.3 Preparation of Sumac Extract

The Sumac fruit extract samples for the antioxidants test were prepared as described previously in Extract Preparation section (Section 3.2).

3.4.2.4 $ABTS^{\bullet+}$ Assay Protocol

The ABTS discoloration assay was conducted to evaluate the potential *in vitro* antioxidant capacity of Sumac extracts, following the protocol by (Qawasmeh, *et al*., 2012).

1. ABTS solution was prepared by dissolving 18 mg of ABTS in 5 mL of distilled water to achieve a concentration of 7 mmol/L.

2. The radical cation ABTS●+ was generated by treating the ABTS solution with 2.45 mmol/L of potassium persulfate (75 mg $K_2S_2O_4$ in 2 mL distilled water). The mixture was allowed to stand in the dark at room temperature for 24 hours, resulting in a dark blue solution.

3. The following day, this solution was diluted until the absorbance reached 0.7 at 734 nm.

4. In plastic cuvettes, 2 mL of the ABTS●+ solution and 30 µL of Sumac extracts (diluted 50-fold) were mixed using a vortex and incubated at room temperature in a dark environment.

5. After 1 hour, the absorbance was measured at 734 nm.

6. Three measurements were taken for each sample.

7. The percentage scavenging of ABTS●+ was calculated using the formula: (Otunola and Afolayan, 2013)

$$ABTS^{\bullet+}\ Scavenging\ (\%) = [(A_{control} - A_{sample}) / A_{control}] \times 100\%$$

Where,

A_{sample}: Sample absorbance and $A_{control}$: Control absorbance

3.5 Determination of Total Polyphenols Content Using Folin–Ciocalteu

The Folin–Ciocalteu method is a widely used technique in analytical chemistry and nutrition science. It helps measure the amount of polyphenols in various substances, including plant extracts. Total phenol contents in Sumac extracts were determined according to the Folin–Ciocaltaeu procedure following the methodology outlined by (Qawasmeh *et al*., 2012).

3.5.1 Preparing Gallic acid as a Stock Solution

The stock solution of Gallic acid was prepared by dissolving 250 mg of G.A. in 5 ml of 80% methanol, chosen due to the insolubility of G.A. in water. This initial solution was then further diluted with distilled water until it reached a final volume of 50 ml. For the Gallic acid calibration curve, concentrations of 50, 100, 150, 250, and 500 mg/L of G.A. were achieved by individually pipetting volumes of 100, 200, 300, 500, and 1000 µl of the stock G.A. solution into separate volumetric flasks. Each flask was subsequently supplemented with distilled water to attain a total volume of 10 ml.

3.5.2 Preparing Na_2CO_3

A sodium carbonate (Na_2CO_3) solution was created by dissolving 20 g of Na_2CO_3 in 80 ml of distilled water with the application of heat. After cooling, the resulting solution was transferred into a volumetric flask and further diluted with distilled water to reach a final volume of 100 ml.

3.5.3 Preparation of Sumac Extract

The Sumac fruit extract samples for total phenols content test were prepared as described previously in Extract Preparation section (Section 3.2).

3.5.4 Folin-Ciocalteu Assay Protocol

Total phenols in Sumac extracts were quantified according to the Folin–Ciocaltaeu procedure following the methodology outlined by (Qawasmeh *et al*., 2012). In this procedure, 20 µl of Sumac extract was combined with 1.58 ml of distilled water and 100 µl of Folin-Ciocalteu reagent. After vortex mixing and a 10-minute incubation in darkness, 300 µl of Na_2CO_3 was added. The cuvettes were then kept in darkness for an hour. Subsequently, the absorbance of the resulting solutions were measured at 760 nm using a spectrophotometer.

To assess Gallic acid solutions' absorbance, the same steps were followed, but for each concentration of Gallic acid solution, 20 µl of G.A. solution was added instead of the plant extract. The resulted absorbance values were used to create a calibration curve with concentration (x-axis) against absorbance (y-axis). This calibration curve was then used to determine the concentration of Sumac extracts. The results were expressed as milligrams of Gallic acid equivalents per gram of dried plant (mg GAE/g dry weight).

3.6 Anticoagulant Activity Screening of *Rhus coriaria* L Extracts

The evaluation of anticoagulant activity in extracts of *Rhus coriaria* L. is a critical exploration in the realm of biomedical research. Anticoagulants are substances that inhibit blood clotting, and their potential presence in Sumac extracts opens avenues for investigating the plant's medicinal properties.

3.6.1 Preparation of Sumac Extract

For the anticoagulation test, Sumac extracts were prepared following a methodology adapted from a previous study involving other plants, with minor modifications (Taj *et al.*, 2016; Taj *et al.*, 2011; Chegu *et al*., 2018). Briefly, one gram of dried local as well as Turkish ground Sumac, was separately suspended in 20 ml of distilled water within conical flasks. These suspensions were left undisturbed for six hours at a temperature of 25°C, facilitated by a shaking incubator. Subsequently, the clear liquid portion of the Sumac extract, known as the supernatant, was isolated through filtration using Whatman filter paper.

The resulting clear solution, constituting a 5% Sumac aqueous extract, was utilized for *in vitro* testing to investigate its potential anticoagulant activity in blood samples obtained from healthy individuals.

3.6.2 Study Population

Blood samples were obtained from five normal volunteers attending the Laboratory at Al-Ramadin Medical Center in Hebron city, Palestine. Both male (n=2) and female (n=3) participants were included to assess the anticoagulant effects of the aqueous extract of *Rhus coriaria* L. The age of the participants ranged between 20 and 50 years old. All participants willingly signed consent forms, demonstrating their complete voluntary participation in the study.

3.6.3 Criteria for Participant Selection

Participants were chosen based on the following criteria:

1. Regular PT values.
2. Absence of cardiovascular conditions (e.g., hypertension, congestive heart failure) and coagulation disorders such as Hemophilia A or B.
3. No history of diabetes.
4. No recent use of nonsteroidal anti-inflammatory drugs (NSAIDs).
5. Non-obesity.
6. Non-alcoholism.
7. Non-smoking.
8. Absence of dyslipidemic disorders.

3.6.4 Collection of Blood Samples

Blood sample collection adhered to the PT and aPTT kit instructions: venous blood was drawn from volunteers' right arms into sterile syringes, transferred into individual test tubes containing sodium citrate as an anticoagulant (at a ratio of 4.5 ml blood to 0.5 ml anticoagulant), and subsequently subjected to 15 minutes of centrifugation at 2500 rpm. This centrifugation isolated blood cells from plasma, yielding pure platelet plasma. All samples underwent PT and aPTT assays within 2 hours of collection, ensuring the reliability of coagulation testing.

3.6.5 *In Vitro* Anticoagulant Tests of Sumac Extract

To evaluate the potential antithrombotic and anticoagulation properties of Sumac, *in vitro* PT and aPTT tests were performed using Sumac plant extracts.

3.6.5.1 Prothrombin Time Test

The PT is a laboratory test used to assess the extrinsic pathway of the blood clotting cascade. It measures the time it takes for plasma to clot after the addition of specific reagents.

1. Determination of Normal PT (Positive Control):

Initially, a plasma sample from each individual was utilized to determine their individual normal PT values followed the protocol outlined in the PT kit instructions. These values served as the positive control group.

2. *In Vitro* Determination of PT with Sumac Extracts:

For the determination of PT for samples with aqueous Sumac extract, the following procedure was followed (Taj *et al.*, 2016**):**

50 µL of normal citrated pure platelet plasma was mixed with varying volumes (50, 75, and 100 µL) of Sumac aqueous extract from each plant extract. This mixture was then gently shaken and incubated at 37°C for one minute in a water bath. Following the incubation period, 200 µL of 10 mM calcium chloride lyophilized rabbit brain thromboplastin reagent (Wiener lab, Argentina) was added to the mixture. This reagent served to counteract the effects of sodium citrate and allow the clotting process to proceed. The time taken for clot formation, known as the prothrombin time, was immediately recorded in seconds using a stopwatch. During this time, the test tubes were gently tilted every 5 seconds to monitor clot formation.

3.6.5.2 Activated Partial Thromboplastin Time Test

The aPTT test assesses the intrinsic and common pathways of the coagulation cascade by measuring the time it takes for blood plasma to clot after the addition of specific activators and calcium ions.

1. Determination of Normal aPPT (Positive Control):

Plasma sample from each individual was utilized to determine their individual normal PT values followed the protocol outlined in the aPPT kit instructions. These values served as the positive control group.

2. *In Vitro* Determination of aPPT with Sumac Extracts:

   Initially, 50 µL of normal citrated pure platelet plasma was incubated with 50 µL of each respective plant extract for 2 minutes at 37 °C in a water bath. Subsequently, 100 µL of the aPTT reagent, comprising a stable aqueous phospholipid suspension with ellagic acid (Wiener lab, Argentina), was added to the mixture. After thorough mixing, the combined solution was incubated for 3 minutes at 37ºC. Following this, 100 µL of a 25 mmol/l calcium chloride solution (Wiener lab, Argentina) preheated to 37°C was introduced. Simultaneously, a stopwatch was initiated, and the tube was briefly shaken for homogenization before being immersed in a water bath for 20 seconds. The tube was then removed from the water bath, and the stopwatch was stopped upon clot formation (Omar *et al.*, 2019).

3.8 High-Performance Liquid Chromatography with Photodiode Array Detection (HPLC-PDA) Analysis

3.8.1 Sample Preparation

1 gram of both dried and fresh Palestinian 1 and Turkish ground Sumac samples underwent two different extraction methods:

1. Room Temperature Extraction: The samples were each mixed with 10 ml of HPLC grade 100% methanol (41722, Carlo Erba, Germany) and allowed to sit for 24 hours at 25°C in a shaking incubator.

2. Reflux Extraction: Another set of samples was mixed with 10 ml of HPLC grade 100% methanol and subjected to a reflux extraction process. This involved refluxing the samples for 24 hours under constant heat until the mixture reached a boiling point.

After the extraction, the resulting extracts were filtered using Whatman filter paper. Subsequently, the suspension was further filtered through a 0.45 µm disposable filter to obtain the final prepared samples for analysis.

3.8.2 Chemicals

Gallic acid, 3,4-dihydroxybenzoic acid, 3,4-dihydroxyphenylacetic acid, chlorogenic acid, 4-hydroxyphenylacetic acid, vanillic acid, caffeic acid, syringic acid, isovanillic acid, p-coumaric acid, ferulic acid, sinapic acid, rutin, verbascoside, quercetin, trans-cinnamic acid, and kaempferol,

3.8.3 Preparation of Reference Standards for HPLC-PDA Analysis

The phytochemical analysis of the Sumac samples was conducted using HPLC-PDA. Seventeen standards for a variety of compounds that mentioned in the chemicals section above, were prepared. These standards were dissolved in 20% ethanol to achieve a concentration of 25 mg per 100 mL. A standard mixture was then created by combining 1.0 mL of each standard solution in a 25 mL volumetric flask, which was subsequently filled to the mark with the same solvent.

3.8.4 HPLC-PDA Instrumentation and Chromatographic Condition

The analysis utilized a gradient elution method to detect the main components in Sumac samples, employing a gradient mobile phase comprising 0.5% acetic acid and acetonitrile **Table 3.1**. Separation was achieved using an RP BDS Hypersil C18 column (Thermo Scientific, 250 x 4.6 mm, 3 µm) with a flow rate set at 0.6 mL/minute. Detection was carried out using a Photodiode Array (PDA) detector, covering a wavelength range from 210 to 400 nm, while the column temperature was maintained at 25°C. Each sample, filtered through a 0.45 µm disposable filter, was injected with a volume of 20 µL for analysis.

Table 3.1: Gradient mobile phase

Time (minutes)	0.5% Acetic acid (%)	Acetonitrile (%)
0	95	5
50	80	20
65	65	35
70	40	60
75	10	90

78	95	5
80	95	5

3.9 Proximate Analysis of *Rhus coriaria L*

Proximate analysis for a fruit sample involves determining its basic composition, typically including moisture content, ash content, fiber content, and crude fat (lipids), as well as carbohydrates. In this study, we measured the moisture content, ash content, fiber content, and crude fat for both the two locally sourced and Turkish-obtained Sumac samples, according to the Association of Official Analytical Chemists (AOAC, 2000) procedure (AOAC,2000).

3.9.1 Moisture Content

The amount of water in the samples of Sumac is determined by drying Sumac samples in a forced-air drying oven at 110°C for 24 hours. The fruit samples are evenly placed on drying racks or trays, ensuring uniform spread to promote even drying. The loss in weight represents the moisture content, calculated using the formula: (AOAC, 2000).

Moisture Content (%) = $[(W_1 - W_2) / W_1] \times 100$

Where:

W_1 = Initial weight of the Sumac sample
W_2 = Weight of the dried Sumac sample

3.9.2 Ash Content

The ash content in Sumac, representing the inorganic components and total minerals in the plant material, was assessed by completely combusting 1 gram of finely powdered Sumac of each sample in a muffle furnace oven set at 550°C. This process ensures uniform combustion and involves the complete oxidation of organic components, including carbon-based compounds, which are converted into gases like carbon dioxide and water vapor. As a result, only the inorganic components remain as ash. This ash serves as the basis for further mineral analysis. The ash percentage was computed using this formula: (AOAC, 2000).

%Ash = ((Weight of test portion - Weight loss on ashing) / Weight of test portion) * 100

3.9.3 Crude Fat

The fat content in Sumac samples was quantified using solvent extraction methods with petroleum ether as the solvent, employing the Soxtherm apparatus (Gerhardt, Germany). This method involved placing approximately 2g of Sumac in a pre-weighed thimble and continuously cycling a solvent (petroleum ether) through the sample (AOAC, 2000). The solvent extracted the fat from the Sumac as it vaporized and condensed. After extraction, the solvent was evaporated, leaving behind a residue that represents the percentage of crude fat in the original sample, which was then weighed to calculate the crude fat percentage.

3.9.4 Fiber Content

Crude fiber analysis was conducted on 1 g samples from each Sumac variety using an Ankom 200 fiber analyzer (USA). The samples underwent digestion with H_2SO_4 (1.25% v/v) at 100°C for 30 minutes, followed by digestion with KOH (1.25%, v/v) at 100°C for another 30 minutes (AOAC, 2000). Subsequently, the Sumac samples were dried at 100°C for 3 hours, and their weights were recorded. This experiment was performed in triplicate.

3.10 Estimation of Minerals in Sumac

In the process of ashing, all organic constituents within the Sumac sample were burned away, resulting in the residue known as ash, primarily composed of inorganic minerals found in the Sumac. This ash was used as the basis for extracting and estimating various minerals in sumac, according to the method proposed by AOAC including sodium (Na), calcium (Ca), potassium (K), magnesium (Mg), and zinc (Zn), as well as estimating the levels of phosphorus (P) and boron (B).

3.10.1 Estimation of Sodium (Na), Calcium (Ca), Potassium (K), Magnesium (Mg), and Zinc (Zn) Levels

The quantification of individual mineral elements in the Sumac sample began with the addition of 10 ml of 2N HCl to each Sumac ash sample for mineral extraction. Afterward, the samples underwent filtration into volumetric flasks. Following filtration, distilled water was added to each flask to reach a final volume of 100 ml.

Subsequently, the absorbance of standard solutions for each mineral was determined, and the absorbance of all the Sumac samples was measured using atomic absorption

spectroscopy (AAS) via a PERKIN ELMER AAnalyst 100 instrument. This measurement process was carried out in triplicate for each sample.

3.10.2 Estimation of Phosphorus (P) Level

To assess the phosphorus content in each Sumac sample, 10 mL of the pre-prepared HCl Sumac ash extract was combined with 10 mL of ammonium vanadomolybdate reagents, known for producing a consistent yellow color when reacting with phosphates. The mixture was then diluted with distilled water to reach a final volume of 100 mL. Subsequently, the absorbance of all samples was measured at 410 nm using a spectrophotometer.

3.10.3 Estimation of Boron (B) Level

To assess the boron content in Sumac, 10 mL of H_2SO_4 (0.36 M) were introduced to the ash samples and allowed to react for one hour. Following this, 1 mL of the suspension was combined with 2 mL of a buffer solution comprising ammonium acetate, EDTA, acetic acid, along with 2 mL of azomethine (H). The mixture was then incubated for 30 minutes. Subsequently, the absorbance of the samples were measured at 420 nm using a spectrophotometer.

Chapter Four: Results

4. Results

4.1 Antibacterial Activity of *Rhus coriaria* L Extracts

The antimicrobial activity of the 18 Sumac extracts, categorized by cultivation source, extraction method, and MeOH concentration, was assessed through the disc diffusion method. Zones of inhibition were measured to determine the efficacy of these extracts against ESBL and MRSA, with Co-Trimoxazole and Meropenem 10 as positive controls **(Figure 4.1)**. The results, as summarized in **Table 4.1** and graphically depicted in **(Figure 4.2, and Figure 4.3)** reveal significant variations in antimicrobial activity across the different extract categories.

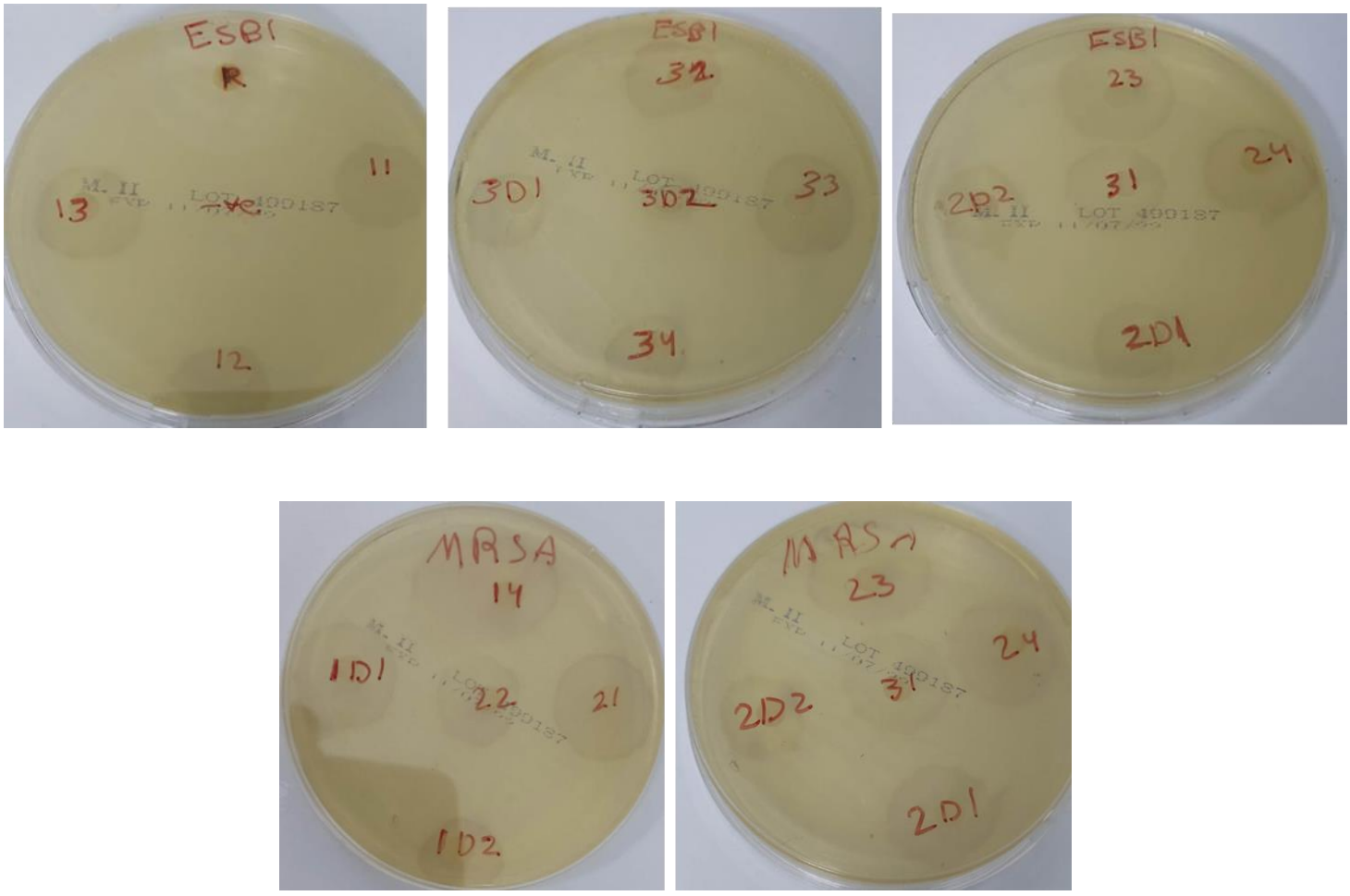

Figure 4.1: Zone of inhibition by some tested Sumac extracts against MRSA and ESBL.

Table 4.1: The antibacterial activity of methanolic extracts of *Rhus coriaria* L.

	ESBL		**MRSA**	
	Inhibition Zone Diameter (mm)	Percent of Inhibition %	Inhibition Zone Diameter (mm)	Percent of Inhibition %
Palestinian1, RT, 100% MeoH	21	30%	20	52.17%
Palestinian1, RT, 80% MeoH	19	23.33%	18	43.48%
Palestinian1, Reflux, 100% MeoH	22	33.33%	30	95.65%
Palestinian1, Reflux, 80% MeoH	25	43.33%	24	69.56%
Palestinian1 Dry, RT, 100% MeoH	20	26.67%	23	65.22%
Palestinian1 Dry, RT, 80% MeoH	20	26.67%	22	60.87%
Palestinian2, RT, 100% MeoH	23	36.67%	24	69.56%
Palestinian2, RT, 80% MeoH	22	33.33%	21	56.52%
Palestinian2, Reflux, 100% MeoH	26	46.67%	27	82.61%
Palestinian2, Reflux, 80% MeoH	24	40%	24	69.56%
Palestinian2 Dry, RT, 100% MeoH	18	20%	23	65.22%
Palestinian2 Dry, RT, 80% MeoH	17	16.67%	22	60.87%
Turkish, RT, 100% MeoH	22	33.33%	25	73.91%
Turkish, RT, 80% MeoH	19	23.33%	24	69.56%
Turkish, Reflux, 100% MeoH	24	40%	25	73.91%
Turkish, Reflux, 80% MeoH	22	33.33%	21	56.52%
Turkish Dry, RT, 100% MeoH	18	20%	23	65.22%
Turkish Dry, RT, 80% MeoH	15	10%	20	52.17%
Negative control (solvent only)	12		8	
Meropenem 10 mcg	30		NT	
Co-Trimoxazole	NT		23	

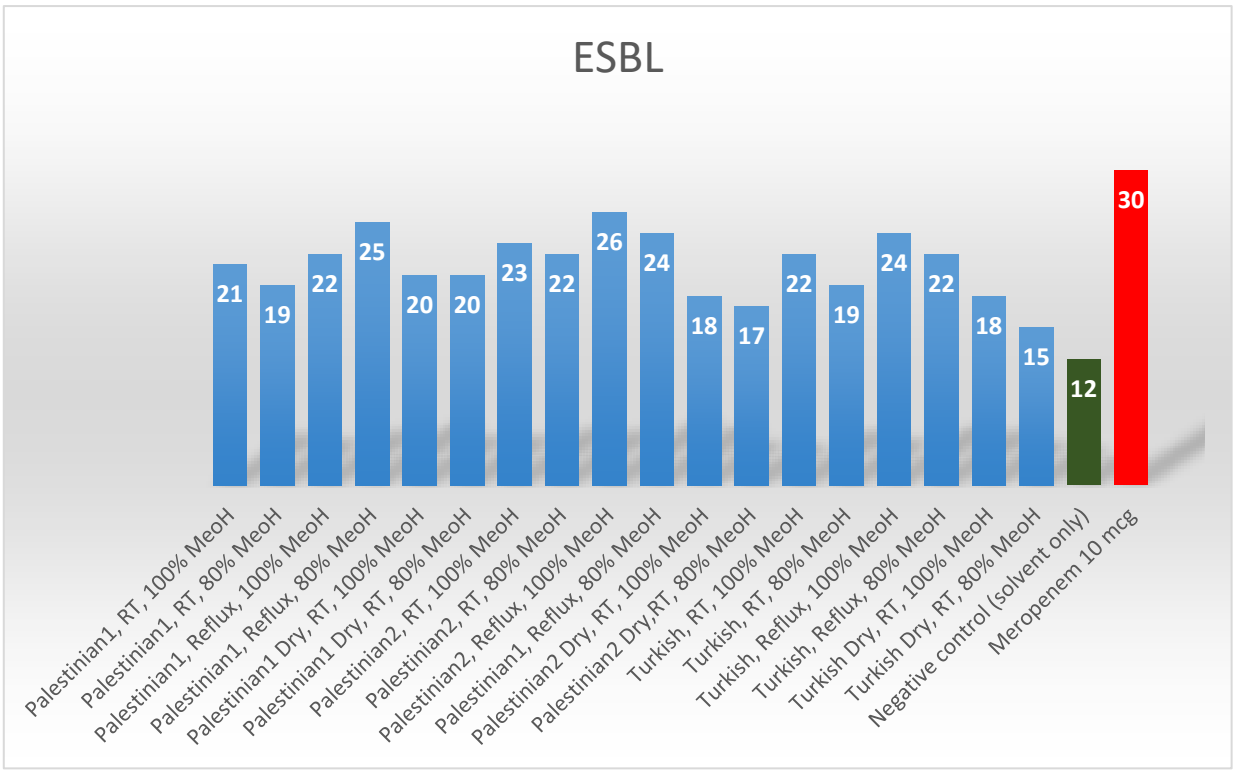

Figure 4.2: The inhibition zone diameter in mm of Rhus coriaria extracts against ESBL bacteria.

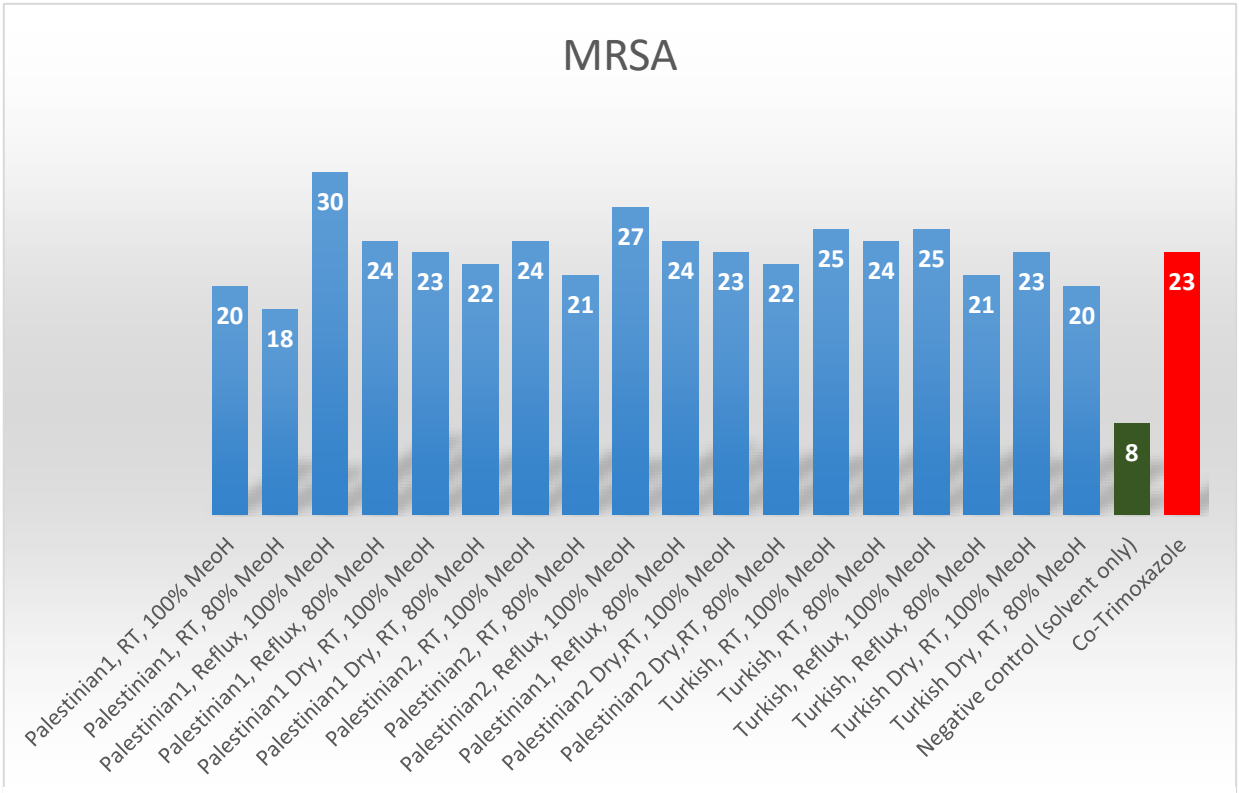

Figure 4.3: The inhibition zone diameter in mm of *Rhus coriaria* extracts against MRSA bacteria.

4.2 Antioxidant Activity of *Rhus coriaria* L Extracts

4.2.1 DPPH• scavenging capacity

Diluted methanol extracts (1:50) from various Sumac samples exhibited significant antioxidant activity, as evaluated through the DPPH• free radical scavenging assay. The average percentage of scavenging of methanolic extracts is presented in the **Table 4.2** and **Figure 4.4**.

Table 4.2: Radical scavenging percentage of *Rhus coriaria* extracts assayed by DPPH radical scavenging method.

DPPH• Scavenging %			
Extraction type and solvent concentration	**Cultivation source**		
	Palestinian 1	**Palestinian 2**	**Turkish**
Room Temp extraction using 100% MeOH	52.40%	37.60%	39.40%
Room Temp extraction using 80% MeOH	45.90%	54.60%	39.40%
Reflux extraction using 100% MeOH	56.20%	70.80%	73.03%
Reflux extraction using 80% MeOH	53.90%	64.90%	50%
Room Temp extraction using 100% MeOH of dried Sumac	44.50%	40.10%	38.30%
Room Temp extraction using 80% MeOH of dried Sumac	52.80%	44.30%	40.20%

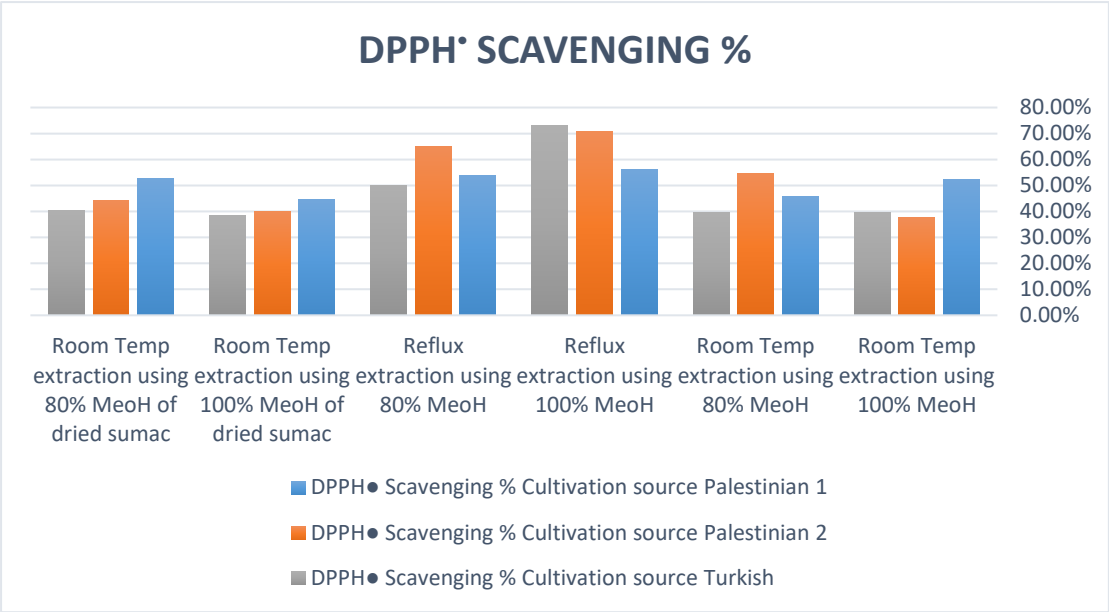

Figure 4.4: The radical scavenging effect of *Rhus coriaria* extracts assayed by DPPH.

4.2.2 $ABTS^{\bullet+}$ scavenging capacity

Diluted methanol extracts (1:50) from various Sumac samples exhibited significant antioxidant activity, as evaluated through the $ABTS^{+\bullet}$ free radical scavenging assay. The average percentage of scavenging of methanolic extracts is presented in **Table 4.3** and **Figure 4.5**

Table 4.3: Radical scavenging percentage of *Rhus coriaria* extracts assayed by ABTS radical scavenging method.

$ABTS^{+\bullet}$ Scavenging %			
Extraction type and solvent concentration	**Cultivation source**		
	Palestinian 1	**Palestinian 2**	**Turkish**
Room Temp extraction using 100% MeOH	29.20%	37%	31.40%
Room Temp extraction using 80% MeOH	32.60%	26 %	28.70%
Reflux extraction using 100% MeOH	52.30%	48.60%	51.70%
Reflux extraction using 80% MeOH	29.60%	40.30%	44.20%
Room Temp extraction using 100% MeOH of dried Sumac	33%	29.20%	30.80%
Room Temp extraction using 80% MeOH of dried Sumac	30.90%	29.30%	37.90%

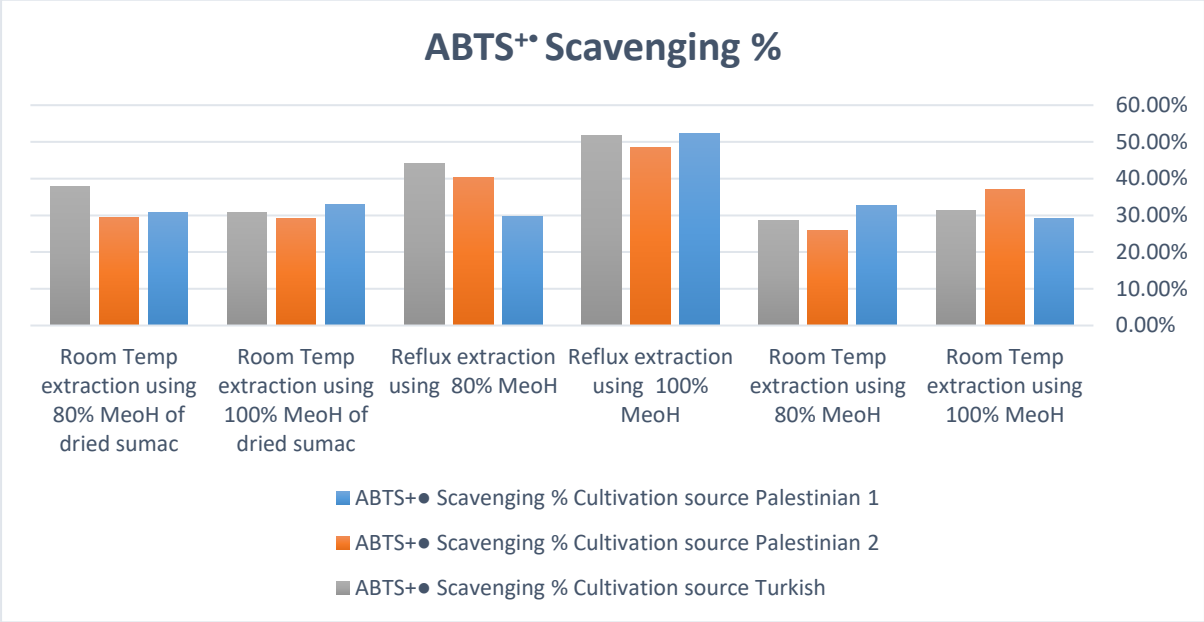

Figure 4.5: The radical scavenging effect of *Rhus coriaria* extracts assayed by ABTS.

4.3 Total Polyphenols Content Using Folin–Ciocalteu

The quantitative estimation of total phenols in the 1:50 diluted methanolic extracts of various Sumac samples was determined in milligrams of Gallic acid equivalent (GAE mg/g), as depicted in **Figure 4.6** and **Table 4.4**.

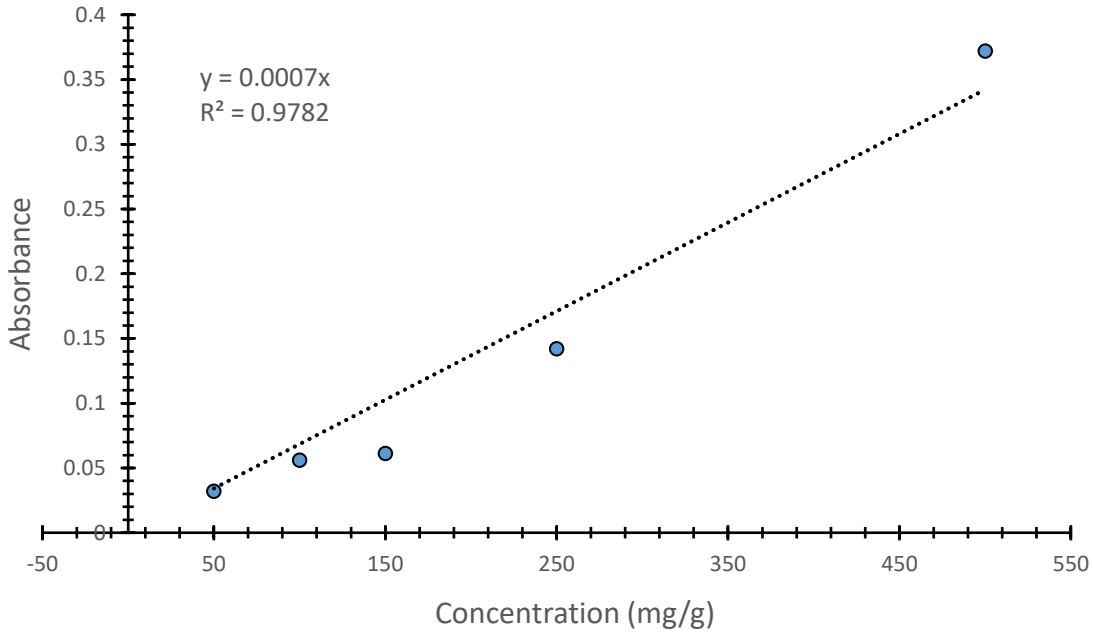

Figure 4.6: Calibration curve of Gallic acid.

Table 4.4: Total phenols of *Rhus coriaria* extracts using Folin-Ciocalteu reagent.

Total Phenol content in mg GAE /g			
Extraction type and solvent concentration	**Cultivation source**		
	Palestinian 1	**Palestinian 2**	**Turkish**
Room Temp extraction using 100% MeOH	226.190	151.428	201.905
Room Temp extraction using 80% MeOH	191.429	131.428	161.905
Reflux extraction using 100% MeOH	315	232.857	352.857
Reflux extraction using 80% MeOH	222.857	210	275.238
Room Temp extraction using 100% MeOH of dried Sumac	210.714	148.09	260.476
Room Temp extraction using 80% MeOH of dried Sumac	168.095	137.143	159.048

4.4 Anticoagulant Activity of *Rhus coriaria* L Extracts

Coagulation assessments were performed using PT and aPTT assays for aqueous extracts of Turkish and Palestinian 1 cultivated Sumac. It's important to note that baseline PT and aPTT values for all participants were within the normal range (13.6 ± 0.05 seconds and 36 ± 1.00 seconds, respectively). However, upon introducing the aqueous Sumac extract (at a 5% concentration) in varying volumes (50, 75, and 100 μL) to plasma samples from healthy individuals, a significant prolongation of aPTT ($P < 0.05$) was observed. Specifically, aPTT increased from 36 ± 1.00 seconds to 49.2 ± 2.43, 51.8 ± 2.47, and 59.6 ± 3.15 seconds for Palestinian cultivated Sumac and from 36 ± 1.00 seconds to 45.2 ± 1.88, 47.2 ± 2.47, and 57.8 ± 2.43 seconds for Turkish Sumac. Notably, the extract had no discernible effect on prothrombin time as shown in **Table 4.5**.

Furthermore, both Turkish and Palestinian Sumac aqueous extracts demonstrated a substantial and statistically significant prolongation effect on aPTT ($P < 0.05$), which was concentration-dependent, as illustrated in **Figure 4.7**. Importantly, there were no statistically significant differences observed when comparing the impact of Turkish and Palestinian Sumac on aPTT ($P > 0.05$).

Table 4.5: Prothrombin time and Activated partial thromboplastin time values of the studied Sumac extracts, illustrating the stastical P values for aPTTvalues

Sample	aPTT test results in (Sec)	*P* Value*	PT test results in (Sec)
Control	36 ± 1.00	-	**13.6 ± 0.05**
Palestinian Sumac (50 µL)	49.2 ±2.43	0.001	**13.6 ± 0.05**
Palestinian Sumac (75 µL)	51.8 ±2.47	0.001	**13.6 ± 0.05**
Palestinian Sumac (100 µL)	59.6 ±3.15	0.002	**13.6 ± 0.05**
Turkish Sumac (50 µL)	45.2 ±1.88	0.002	**13.6 ± 0.05**
Turkish Sumac (75 µL)	47.2 ±2.47	0.003	**13.6 ± 0.05**
Turkish Sumac (100 µL)	57.8 ±2.43	0.002	**13.6 ± 0.05**

*p value <0.05 was significant relative to the control (blood sample without plant extract). PT: Prothrombin time, aPTT: Activated partial thromboplastin time

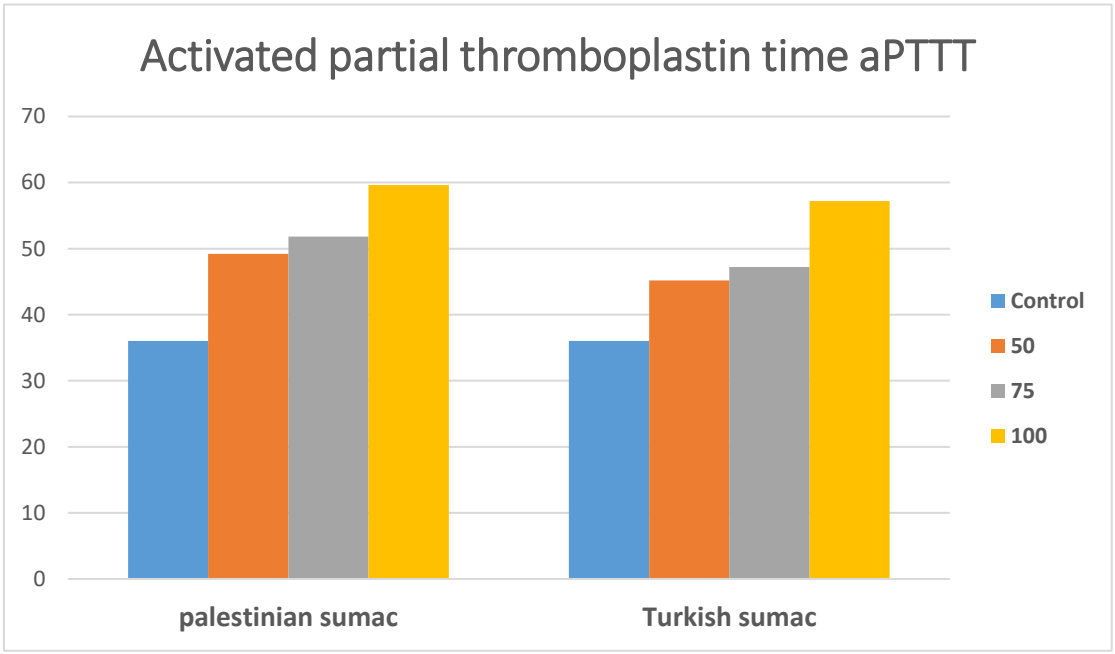

Figure 4.7: The effect of different volumes of aqueous exctracts of Palestinian and Turkish Sumac on aPTT of plasma samples.

4.6 High-Performance Liquid Chromatography with Photodiode Array Detection (HPLC-PDA) Analysis

HPLC analysis was conducted on Turkish and Palestinian 1 Sumac samples that were extracted using 100% MeOH, with samples extracted using 80% MeOH excluded from the analysis.

Seventeen standards of flavonoids and phenolic compounds were separated in different retention times, each corresponding to a specific number in **Figure 4.8**, 1: Gallic acid, 2: 3, 4-dihydroxybenzoic acid, 3: 3, 4-dihydroxyphenylacetic acid, 4: Chlorogenic acid, 5: 4-hydroxyphenylacetic acid, 6: Vanillic acid, 7: Caffeic acid, 8: Syringic acid, 9: Isovanillic acid, 10: *p*-coumaric acid, 11: Ferulic acid, 12: Sinapic acid, 13: Rutin, 14: Verbascoside, 15: Quercetin, 16: *trans*-cinnamic acid, and 17: Kaempferol. This particular chromatogram was selected because it displayed all the standards at 280 nm, despite each having a different maximum wavelength.

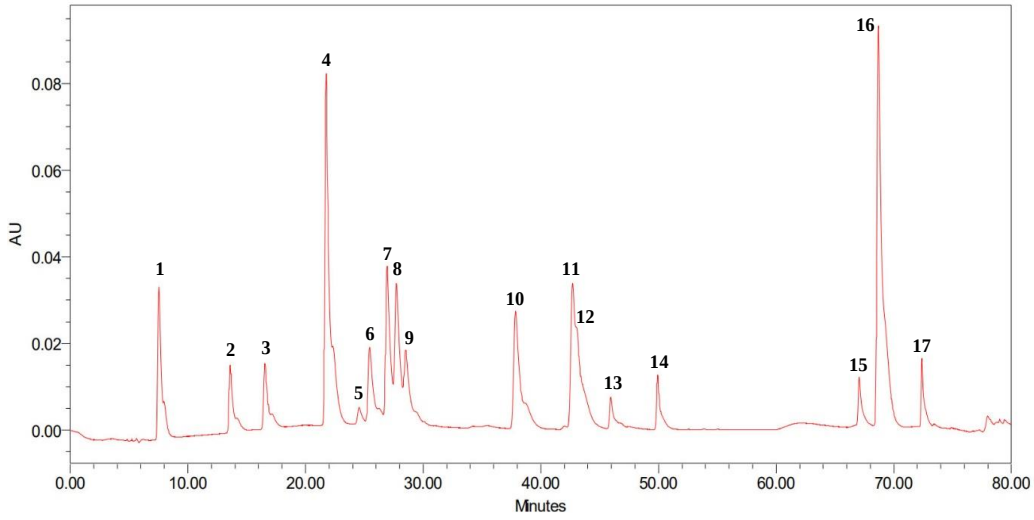

Figure 4.8: HPLC chromatogram for standards used at 280nm.

The HPLC results were presented in selective chromatograms. **Figure 4.9** illustrates the chromatogram for dried Palestinian 1 Sumac extracted with 100% methanol at 280 nm, while **Figure 4.10** showcases the chromatogram for dried Turkish Sumac extracted with 100% methanol at 280 nm. Identification of compounds was based on their retention times and wavelengths, aligning them with standards and sample peaks. Consequently, the following compounds were identified: In dried Palestinian 1, Gallic acid and Rutin with retention times of 7.73 and 47.57 minutes, respectively. In dried

Turkish Sumac, Gallic acid at a retention time of 7.755 minutes and Rutin at 47.675 minutes were identified.

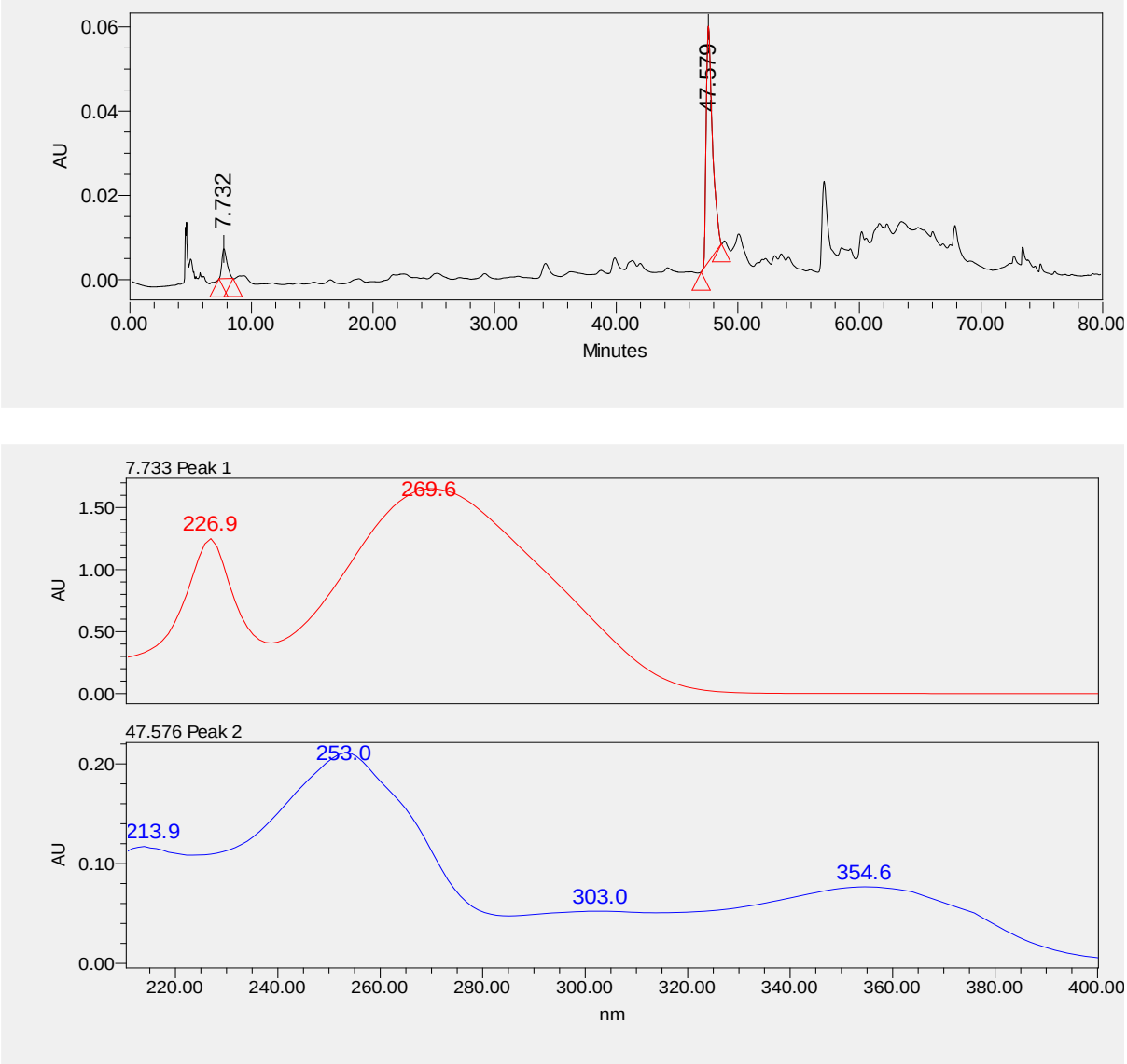

Figure 4.9: HPLC chromatogram for dried Palestinian1 Sumac extracted with 100% MeOH at 280nm and UV spectrum for the two main peaks.

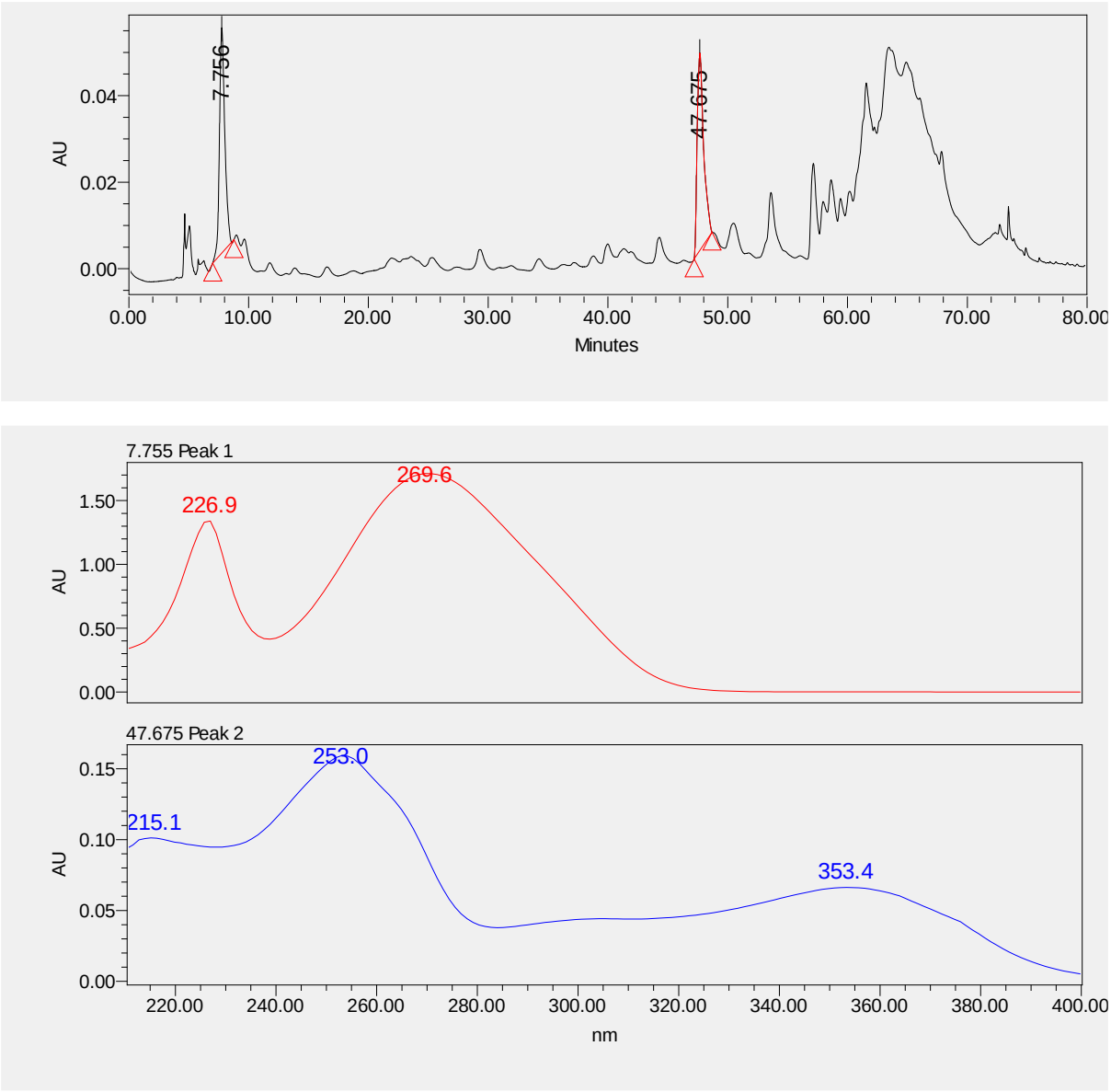

Figure 4.10: HPLC chromatogram for dried Turkish Sumac extracted with 100% MeOH at 280nm and UV spectrum for the two main peaks.

4.7 Proximate Analysis of *Rhus coriaria L*

Table 4.6 provides a summary of the results of proximate analysis for Turkish and Palestinian cultivated Sumac, encompassing moisture content (%), ash content (%), fat content (%), fiber content (%), and dry matter (%). These values represent the mean of triplicate determinations in the analysis.

Table 4.6: Proximate parameters of *Rhus coriaria* L.

	Moisture %	Dry matter %	Ash %	Fiber %	Fat %
Palestinian 1	8.69%	91.31%	2.8%	35.67%	23.19%
Palestinian 2	10.09%	89.91%	3.4%	34.90%	21.83%
Turkish	6.29%	93.71%	2.6%	37.06%	22.71%

4.8 Minerals compositions of *Rhus coriaria L*

The mineral composition of all the examined Sumac extracts showed in **Table 4.7** and illustrated in **Figure 4.11**).

Table 4.7: Minerals composition of *Rhus coriaria* L.

	Potassium	Calcium	Magnesium	Sodium	Boron	Phosphorus	Zinc
Palestinian 1	6385	3042	2758	475	492.6	174.2	55.9
Palestinian2	6997	3440	2959	537	604.4	282.3	53.7
Turkish	6881	3403	2789	534	521.5	263	47.8

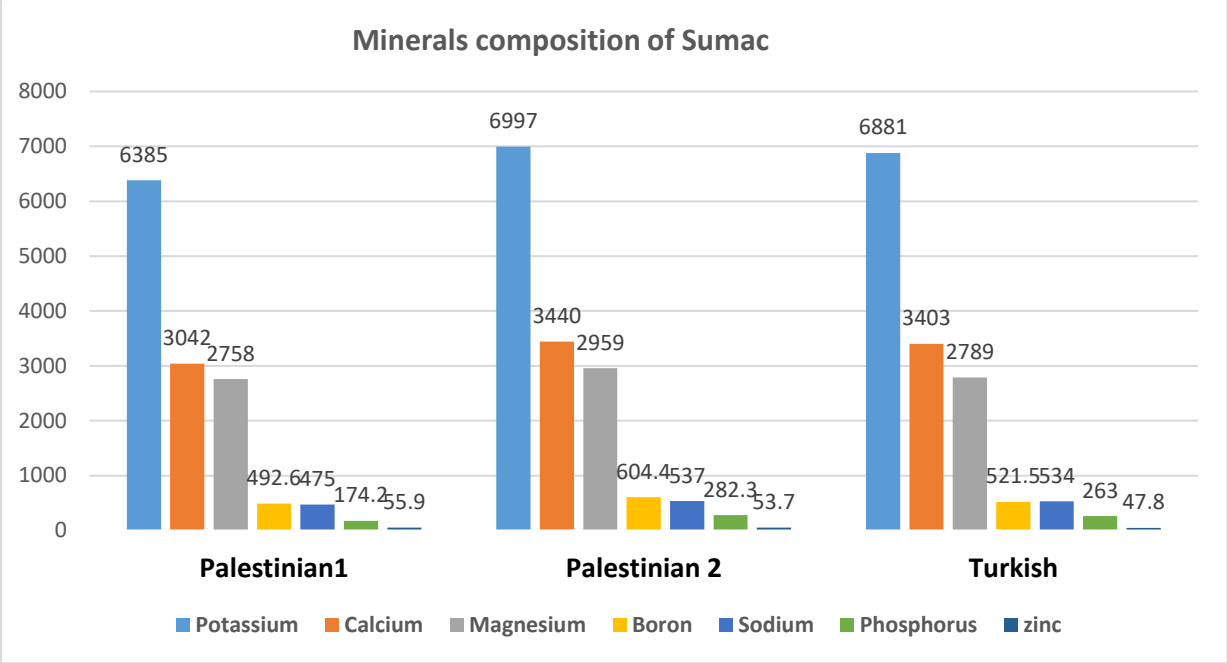

Figure 4.11: Minerals composition of *Rhus coriaria* L.

Chapter Five: Discussion

5. Discussion

This study delved into the multifaceted potential of *Rhus coriaria* fruits in Palestinian cuisine, marking the first exploration of Sumac extract's impact on coagulopathy. We comprehensively assessed its diverse biological properties, including antioxidant capabilities, antibacterial activities, phytochemical composition, *in vitro* anticoagulation, and proximate analysis, covering extracts from both Palestinian and Turkish origins.

The misuse of antibiotics has led to the emergence of drug-resistant strains, notably MRSA, contributing significantly to high mortality rates in antimicrobial-resistant infections worldwide (Salam *et al*., 2023). Our study aimed to assess the *in vitro* antibacterial activity of *Rhus coriaria* extracts against drug-resistant strains, including gram-positive MRSA and gram-negative ESBL strains. Remarkable antibacterial efficacy was observed for both Palestinian and Turkish Sumac extracts against these strains, reaffirming the broad-spectrum antibacterial effects of methanolic extracts from Sumac against diverse bacterial strains of both gram-positive and gram-negative bacteria (Ghane *et al*., 2022; Naik *et al*., 2021; Gabr and Alghadir, 2019; Adwan *et al*., 2015). Palestinian 1 extracts inhibited MRSA between 43.48% and 95.65% and ESBL between 23.33% and 43.33%, while Palestinian 2 extracts inhibited MRSA between 56.52% and 82.61% and ESBL between 16.6% and 46.67%. Turkish Sumac extracts displayed inhibition against MRSA between 52.17% and 73.91% and against ESBL between 10% and 40%. Notably, extracts prepared using 100% methanol exhibited higher antibacterial potential compared to those containing 80% methanol concentration, indicating methanol's superior ability to extract flavonoids and phenolics from Sumac. Additionally, the reflux method showed the most substantial inhibition zones against both MRSA and ESBL, underscoring the effectiveness of moderate heat treatment in isolating bioactive components responsible for antibacterial activity.

Our investigation into *Rhus coriaria* fruits expanded beyond antibacterial activities to evaluate antioxidant capacity and total phenolic content. Using established spectrophotometric assays like DPPH and ABTS+, we explored the antioxidant activity and scavenging potential of *Rhus coriaria* extracts, essential in understanding their therapeutic potential against conditions linked to oxidative stress.

Our findings indicate variation in antioxidant activities across different Sumac extracts, influenced by extraction methods and geographical origins. Diluted methanol extracts (1:50) exhibited % DPPH scavenging ranging from 44.5% to 56.2% for Palestinian 1, 37.6% to 70.8% for Palestinian 2, and 38.3% to 73.03% for Turkish extracts. % ABTS scavenging varied between 29.2% to 52.3% for Palestinian 1, 26% to 48.6% for Palestinian 2, and 28.7% to 51.7% for Turkish extracts. Total phenolic content varied among diluted Sumac samples, with Palestinian 2 exhibiting slightly lower total phenolic content across all extraction methods and solvent concentrations, contrasting Palestinian 1 and Turkish Sumac, which demonstrated similar total phenolic levels. The highest total phenolic content was identified in Turkish Sumac extracted with 100% methanol using the reflux method, registering at 352.857 mg GAE/g followed by Palestinian 1 Sumac extracted in the same way registering at 315 mg GAE/g. The highest phenol contents and percentages of scavenging were consistently observed in reflux-extracted using 100% methanol extracts, indicating the effectiveness of methanol in isolating bioactive components such as phenolic compounds responsible for antioxidants activity also enhanced antioxidant potential and phenolic content of Sumac by increased temperature in reflux extraction, suggesting that increased temperature positively influences solubility and mass transfer rate.

Various studies have showcased a wide range of antioxidant capacities and total phenolic contents in Sumac extracts, corroborating our findings. For instance, Alwazeer and Sally (2019) reported DPPH scavenging activities of Sumac water extracts ranging from 75.29% to 84.84% (Alwazeer and Sally, 2019), while Bursal and Köksal (2011) observed scavenging activities at 41.2% (Bursal and Köksal, 2011). Similarly, Taskin *et al*. (2020) noted varying phenolic contents in Sumac leaves extracted using different solvents (Taskin *et al*., 2020). Fereidoonfar *et al*. (2019) revealed substantial disparity in phenolic content ranged from 77.54 to 389.30 mg GAE/g among Sumac accessions (Fereidoonfar *et al.*, 2019), while Ozcan *et al*. (2021) showcasing total antioxidant values ranging narrowly from 73.37% to 77.00% and total phenolic content varying from 36.38 to 58.66 mg/g among Turkish Sumac genotypes (Ozcan *et al*., 2021).. These findings underscore the complexity of antioxidant capacities and phenolic contents in Sumac extracts, influenced by extraction methods, solvents, geographic origin, and genetic diversity among Sumac genotypes.

Our study sheds light on Sumac's potential in understanding the blood coagulation cascade, vital for hemostasis maintenance. By examining the intrinsic and extrinsic pathways converging into factor Xa activation, leading to thrombin generation and fibrin formation (Krishnaswamy, 2013; Yan *et al*., 2018), our investigation introduces a novel perspective on Sumac's hemostatic properties, expanding upon previous studies on various plant species such as *Zingiber officinale* rhizomes, *Allium Sativum* Plant, Red Onion, and other medicinal plants (Taj *et al*., 2016; Padh and Patel, 2001; *Taj et al*., 2011; Abdallah *et al*., 2022; Omar *et al*., 2019; Chegu *et al*., 2018). Through PT and aPTT assays, we uniquely assess Sumac's impact on the coagulation pathways, offering valuable insights into its potential therapeutic applications.

Significantly, when introducing the aqueous Sumac extract (at a 5% concentration) in varying volumes (50, 75, and 100 μL) to plasma samples from healthy individuals, we observed a statistically significant prolongation of aPTT ($P < 0.05$). Palestinian cultivated Sumac exhibited increased aPTT from 36 ± 1.00 seconds to 49.2 ± 2.43, 51.8 ± 2.47, and 59.6 ± 3.15 seconds, whereas Turkish Sumac prolonged aPTT from 36 ± 1.00 seconds to 45.2 ± 1.88, 47.2 ± 2.47, and 57.8 ± 2.43 seconds. Interestingly, the extract did not impact prothrombin time. These findings indicate the potential of aqueous Sumac extract to modulate the intrinsic coagulation pathway without affecting the extrinsic pathway, underscoring its promising hemostatic properties that warrant further investigation.

Moreover, both Turkish and Palestinian Sumac aqueous extracts displayed concentration-dependent substantial prolongation effects on aPTT ($P < 0.05$). Importantly, no statistically significant differences were noted in comparing the impact of Turkish and Palestinian Sumac on aPTT ($P > 0.05$). These results indicate the consistent and concentration-related influence of Sumac extracts on the intrinsic coagulation pathway, irrespective of geographic origin, emphasizing the reproducibility of their hemostatic effects.

The HPLC analysis in our study provided valuable insights into the flavonoids and phenolic compounds present in Turkish and Palestinian 1 Sumac extracts. Exclusion of samples extracted with 80% MeOH ensured focused analysis, enhancing compound identification accuracy.

Gallic acid and Rutin were identified in both extracts, indicating their potential health benefits. In the dried Palestinian 1 Sumac extract, Gallic acid and Rutin were successfully identified with retention times of 7.73 and 47.57 minutes, respectively. Similarly, the dried Turkish Sumac extract exhibited the presence of Gallic acid at a retention time of 7.755 minutes and Rutin at 47.675 minutes.While both extracts shared these compounds, subtle differences in retention times suggest variations in concentrations or structures, highlighting their similar compound profiles. Previous studies have demonstrated Sumac's rich polyphenolic composition, including gallic acid derivatives and quercetin, with unique chemical profiles and abundant hydrolysable tannins (Arena *et al*., 2022). Further research (Kosar *et al*., 2007) revealed anthocyanins and hydrolysable tannins in Sumac, with gallic acid being predominant.

The proximate analysis of Sumac conducted in this study provides a comprehensive understanding of its basic composition, encompassing moisture, dry matter, ash, fiber, and crude fat. These parameters are essential for assessing its nutritional and potential therapeutic value.

The moisture content varied across Sumac samples, closely matching earlier reports (6–11.8%) (Ozcan and Haciseferogullari, 2004; Dogan and Akgul, 2005; Kizil and Turk, 2010), with Palestinian 1 at 8.69%, Palestinian 2 at 10.09%, and Turkish Sumac at 6.29%. Turning to ash content, values for Palestinian 1 (2.8%), Palestinian 2 (3.4%), and Turkish Sumac (2.6%) align closely with earlier reports as 2.93% by Raodah *et al*. (2014) and from 2.8% to 3.3% by Dogan and Akgul (2005).

Concerning fiber, the observed values of 35.67% (Palestinian 1), 34.90% (Palestinian 2), and 37.06% (Turkish Sumac) are consistent with reported fiber content in Sumac fruits at 33.21% (Vecchio *et al*., 2022). The crude fat content of Sumac, ranging from 21.83% to 23.19% in our study, represents the second most abundant compound in Sumac, consistent with previous reports. However, it is slightly higher compared to values of 9.56%, 18.74%, and 17.4% reported by Vecchio *et al*. (2022), Raodah *et al*. (2014), and Kizil and Turk (2010), respectively. The high dry matter content, reflecting the residual after moisture removal, highlights Sumac's potential as a nutrient-rich food source. Values for Palestinian 1 (91.31%), Palestinian 2 (89.91%), and Turkish Sumac (93.71%) signify a concentration of essential components.

Turning to the mineral composition in Sumac, the analysis of all examined Sumac extracts revealed remarkable similarities in their elemental content. Potassium emerged as the most prevalent element, with concentrations of 6385 ppm (Palestinian 1), 6997 ppm (Palestinian 2), and 6881 ppm (Turkish Sumac). Calcium was also present in substantial amounts, registering at concentrations of 3042 ppm (Palestinian 1), 3440 ppm (Palestinian 2), and 3403 ppm (Turkish Sumac). On the other hand, zinc exhibited the lowest concentration among the analyzed minerals at around 55.9 ppm. Our findings align with previous studies, emphasizing the prevalence of minerals such as potassium, calcium, and magnesium in Sumac. Kizil and Turk (2010) reported potassium (5259.0 ppm), calcium (1334.7 ppm), and magnesium (765.8 ppm) as major micronutrients. Similarly, Ozcan and Haciseferogullari (2004) identified potassium (7963.5 ppm) and calcium (3661 ppm) as predominant elements. Vecchio *et al*. (2022) also confirmed the abundance of potassium, calcium, magnesium, and phosphorus in Sumac.

The comparative analysis between Palestinian and Turkish Sumac sources reveals slight differences in various biochemical activities. Palestinian Sumac consistently demonstrates generally comparable or slightly higher inhibition zone diameters against ESBL and MRSA strains in antibacterial efficacy. In radical scavenging activities, Palestinian Sumac exhibits superior scavenging percentages in DPPH, except for reflux extraction using 100% MeOH, whereas Turkish Sumac showed higher percentages. In ABTS+ assays, Turkish Sumac consistently demonstrates comparable or slightly higher values. Regarding total phenol content, Turkish Sumac extracts generally show higher values, notably in reflux extraction with 100% MeOH. Both Turkish and Palestinian Sumac sources display significant prolongation of aPTT, indicating hemostatic potential, with no statistically significant differences observed between them. Furthermore, both sources share specific compounds like Gallic acid and Rutin in their profiles, suggesting overall bioactivity and functional similarity. Subtle variations in proximate parameters are noted, with Turkish Sumac exhibiting higher fat content and lower moisture. In minerals estimation, there are approximately no differences between Turkish and Palestinian Sumac extracts.

Chapter Six: Conclusion

6. Conclusion

In conclusion, our comprehensive investigation of *Rhus coriaria* (Sumac) fruits has unveiled valuable insights. This study is pioneering in its examination of the potential therapeutic effects of Sumac extract on coagulopathy demonstrating significant ($P < 0.05$) aPTT prolongation in Palestinian and Turkish aqueous extracts from 36 seconds up to 59.6 seconds in Palestinian and up to 57.8 seconds in Turkish extracts, without affecting prothrombin time, indicating a modulatory effect on the intrinsic coagulation pathway and prompting further exploration into Sumac's hemostatic properties.

Furthermore, Palestinian and Turkish Sumac extracts exhibit potent antibacterial efficacy against multidrug-resistant strains, particularly gram-positive MRSA, with Palestinian extracts showing up to 95.65% inhibition addressing global concerns about antimicrobial resistance.

The assessment of antioxidant activities uncovered potent capacities in Sumac extracts, accompanied by variations among samples. Notably influenced by extraction methods solvent concentration, and heat treatment. The utilization of reflux extraction with 100% methanol consistently enhances antioxidant potential and phenol content, underscoring the positive impact of elevated temperature on the extraction efficiency of bioactive constituents.

In our comparative analysis between Turkish and Palestinian Sumac sources, several key findings emerge, shedding light on the similarities and subtle differences in their biochemical activities and nutritional composition. Firstly, the HPLC analysis reveals shared compounds like gallic acid and rutin between Palestinian 1 and Turkish Sumac extracts, indicating a potential uniformity in their biological activities. Secondly, while Palestinian Sumac demonstrates comparable antibacterial efficacy and superior radical scavenging under certain conditions, Turkish Sumac exhibits a higher total phenol content. Nevertheless, both Palestinian and Turkish Sumac sources exhibit hemostatic potential, this suggests that despite minor variations, Sumac from different regions possesses consistent medicinal properties. Furthermore, subtle differences in proximate parameters and minerals estimation hint at distinct nutritional profiles between Palestinian and Turkish Sumac extracts. These variations, while minor, contribute to a

nuanced understanding of Sumac's nutritional composition and may have implications for its utilization in different culinary and medicinal contexts.

Overall, our findings collectively contribute to a deeper understanding of Sumac's multifunctional properties and underscore its potential applications in various fields, including food, medicine, and nutraceuticals. Further research and exploration are warranted to fully elucidate the therapeutic mechanisms of Sumac and to unlock its full potential for human health and well-being.

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Abstract in Arabic

الأنشطة البيولوجية والتركيب الغذائي لنبات السماق. (*Rhus coriaria* L)

الملخص:

السماق (Anacardiaceae) *Rhus coriaria* L، هو من التوابل والبهارات والمنكهات شائعة الاستخدام، خاصة
في منطقة البحر الأبيض المتوسط. نظرًا لقيمته المفيدة الوفيرة، فقد تم استخدام السماق في الطب التقليدي لإدارة وعلاج العديد من الأمراض بما في ذلك البواسير، وشفاء الجروح، والإسهال، والقرحة، والتهاب العين. هذا النبات غني بفئات مختلفة من المواد الكيميائية النباتية بما في ذلك مركبات الفلافونويد والعفص ومركبات البوليفينولوالأحماض العضوية وغيرها الكثير. تقدم هذه الدراسة استكشافًا شاملاً للأنشطة البيوكيميائية والتطبيقات العلاجيةالمحتملة لثمار *Rhus coriaria* (السماق)، التي تعد جزءًا لا يتجزأ من تراث الطهي الفلسطيني. وبدافع من انتشاراستخدام السماق في الأطباق الفلسطينية التقليدية وإمكاناته كمكون وظيفي، إلى جانب ندرة الدراسات حول مستخلصات السماق الفلسطيني، تم إدراج السماق التركي للمقارنة. الهدف الشامل هو دراسة وتقييم الأنشطة البيولوجية والتركيب الغذائي لثمار *Rhus coriaria*، وعلى وجه التحديد تقييم الأنشطة المضادة للبكتيريا ،وخصائص مضادات الأكسدة، ومحتويات الفينول الإجمالية، ومنع تخثر الدم في المختبر، وتحليل HPLC-PDA، والتركيب التقريبي، وتقدير المعادن للفلسطينيين والتركيين .- مستخلصات فاكهة السماق المزروعة.

أظهرت النتائج فعالية مضادة للجراثيم ملحوظة لكل من السماق الفلسطيني والتركي ضد السلالات المقاومة للأدوية،وتحديداً MRSA إيجابية الجرام، حيث أظهرت المستخلصات الفلسطينية تثبيطًا يصل إلى 65.95% والمستخلصات التركية تظهر 91.73%. يكشف تقييم خصائص مضادات الأكسدة ومحتوى الفينول الإجمالي أن الاستخلاص الارتجاعي باستخدام الميثانول بنسبة 100% يظُهر باستمرار إمكانات مضادات الأكسدة المحسنة في كل من السماق الفلسطيني والتركي. يمكن أن تعزى الفعالية الفائقة لطريقة استخلاص الميثانول الراجع بنسبة 100% على 80% من الميثانول وطرق استخلاص الميثانول في درجة حرارة الغرفة إلى قابلية ذوبان الميثانول العالية وكفاءة استخلاصه في درجات حرارة مرتفعة، مما يعزز إطلاق المركبات الفينولية وغيرها من المكوناتالنشطة بيولوجيًا المسؤولة عن عملية استخلاص الميثانول. الأنشطة البيولوجية التي تم اختبارها.

تبحث الدراسة أيضًا في إمكانات السماق كمضاد طبيعي للتخثر. تكشف النتائج عن إطالة كبيرة (P <0.05) تعتمدعلى التركيز لزمن الثرومبوبلاستين الجزئي المنشط (aPTT) بواسطة مستخلصات السماق الفلسطينية والتركية،مما يشير إلى تأثير محدد على مسار التخثر الداخلي مع الحفاظ على المسار الخارجي بالمستخلصات الفلسطينية التي تطيل زمن الثرومبوبلاستين الجزئي. تصل إلى 6.59 ثانية والمستخلصات التركية تصل إلى 8.57 ثانية. حدد تحليل HPLC الملامح المركبة المشتركة في

المستخلصات الفلسطينية والتركية، بما في ذلك حمض الغاليك والروتين، مما يشير إلى التوحيد في الأنشطة البيولوجية.

وكشف التحليل المعدني أن البوتاسيوم هو المعدن الأكثر وفرة، بتركيزات تصل إلى 6997 جزء في المليون، يليهالكالسيوم، بتركيزات تصل إلى 3440 جزء في المليون، والمغنيسيوم، بتركيزات تصل إلى 2959 جزء فيالمليون، وكان الزنك موجودا في أقل التركيزات، حيث تم قياسها بحوالي 2959 جزء في المليون. 9.55 جزء في المليون. يكشف التحليل التقريبي أن مستخلصات السماق الفلسطينية والتركية غنية بالألياف، يليها محتوى الدهونوالرطوبة.

على الرغم من بعض الاختلافات، فإن كلا المصدرين يشتركان في إمكانات مرقئية كبيرة ومركبات نشطة بيولوجيًامحددة، مما يؤكد التشابه الوظيفي العام بينهما. ولوحظت اختلافات طفيفة في المعلمات التقريبية، حيث أظهرالسماق التركي محتوى أعلى من الدهون ومحتوى رطوبة أقل. أظهر التقدير المعدني عدم وجود فروق ذات دلالة إحصائية بين مستخلصات السماق التركية والفلسطينية، مما يؤكد النشاط الحيوي الشامل والتشابه الوظيفي.

Appendix

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نموذج موافقة على سحب عينة دم

يُطلب منك المشاركة التطوعية في بحث علمي لدراسة تأثير مستخلص نبات السماق على تخثر الدم. المشاركة في هذه الدراسة البحثية إختيارية. إذا كنت ترغب في المشاركة يرجى قراءة المعلومات التالية حول الدراسة:

- تهدف هذه الدراسة لفحص تأثير مستخلص نبات السماق كمميع للدم، وذلك استكمالاً لمتطلبات الحصول على درجة الماجستير في علوم النباتات والعقاقير الطبية.
- في حال وافقت على المشاركة في هذه الدراسة، فسوف تعطي عينة من دمك لإستخدامها في إجراء فحوصات التخثر، سيتم سحب الدم عن طريق إدخال إبرة في وريد في ذراعك، سيتم أخذ أنبوب دم صغير.
- بمجرد الانتهاء من الفحص باستخدام العينات الخاصة بك، سيتم التخلص منها ولن تستخدم لأي غرض آخر.
- عملية سحب الدم آمنة تماماً ولا توجد أي مخاطر حقيقية محتملة. قد يكون هناك خطر ضئيل للإصابة بكدمات وإغماء.
- لن يتم الإفصاح عن أي معلومات شخصية لاي طرف كان, مثل لن يتم مشاركة اسمك أو أي من معلومات شخصية أخرى.
- المشاركة في هذا البحث العلمي طوعي؛ أي يحق لك قبول إجرائه أو رفضه.

أوافق على أن أشارك في هذه الدراسة بطوعية وبدون أي نوع من الاجبار أو الضغوط. لقد حصلت على شرح مفصل عن الدراسة وأهدافها وإجراءاتها، ومنافعها، والمخاطر المحتملة وعن الحرية الكاملة للمشاركة.

الاسم:

العمر والجنس:

التوقيع:

التاريخ: