Effects of Roselle or Tamarind Extracts and their Mixer versus Potassium Bromate-Induced Nephrotoxicity in Rats

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ABSTRACT

Potassium bromates, still used as food additives and found as a byproduct in ozonate-disinfected water, induced oxidative stress related to nephrotoxicity and pathogenesis of many chronic diseases. Among the countries with the greatest incidence of kidney dysfunction-related fatalities is Egypt. Thus, this investigation aimed to compare the kidney-protective activities of aqueous and alcoholic extracts for tamarind and roselle, individually and in combination, in the presence of potassium bromate-induced nephrotoxic rodents. 48 rats were classified into 8 groups and received potassium bromate as 20 mg /kg b.wt., orally twice a week for 4 weeks alone or combined with different tested extracts daily at 40 mg/ kg b.wt. The tested extracts exhibited reno-protective roles characterized by lowering serum creatinine, urea, uric acid, and urinary protein plus increasing serum total protein, albumin, and clearance of creatinine and uric acid. The significant effects detected for tamarind and mix different extracts especially alcoholic ones, while roselle extracts may need the highest dose and/or period than that used in this study. The extracts' reno-protective action attributed to phenolic compound activities such as antioxidant, antihyperlipidemia, antiatherosclerosis plus inhibition renal lipids and DNA oxidation as malondialdehyde and 8-hydroxydeoxyguanosine (8-OH-dG) results showed. Extracts also showed hepatoprotective effects. Therefore, it is necessary to enhance the use of these plants, fresh or dried, either as beverages or food supplementation as coloring and flavoring agents or therapeutic formulae, or even in general cooking as usually used in many countries. Further searches are needed to detect the ideal safe dose and usage duration.

Keywords: *Hibiscus sabdariffa*, *Tamarindus indica*, kidney function, lipids profile.

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INTRODUCTION

Renal disease be the most prevalent cause of years of life lost globally by 2040 anticipated fifth, with approximately 850 million individuals worldwide predicted to have the condition (**Francis et al., 2024**). The number of fatalities associated with kidney dysfunction in the Middle East and North Africa region was about 2.5 times higher in 2019 than it was in 1990, and the greatest rates were observed in Afghanistan, Egypt, and Saudi Arabia (**Rashidi et al., 2024**). Furthermore, elevated risk of developing non-communicable diseases such as hypertension, ischemic heart illness, peripheral vascular illness, stroke, malignancy, diabetes, and gout is frequently associated with renal disease. Therefore, renal disease management is significantly restricted by the controlling of these conditions and the opposite is true (**Francis *et al.,* 2024; Rashidi *et al.,* 2024**).

Nephrotoxicity is the term used to describe the rapid decline in kidney function that is caused by the toxic effects of both medications and toxins **(Perazella and Rosner, 2022).** Nephrotoxins are substances displaying nephrotoxicity as molds, chemo-therapy drugs, antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), metals, and chemicals that can cause nephrotoxicity. The pharma-ceutical and cosmetic industries frequently employ potassium bromate ($KBrO_3$), an oxidizing agent (e.g., permanent hair weaving solutions and textile dyeing), derived from chemicals that exhibit nephrotoxicity. It is also detected in potable water samples as a byproduct of ozone disinfection **(Abd El-Rahim *et al.,* 2018).** However, in numerous countries, it has been linked to the development of multiple organ injuries, it is still used as a food additive, whether legally or illegally, in cakes, bread, cheese, beer, and fish paste products production **(Abdel-Latif *et al.*, 2021**). The development of numerous renal and nonrenal tumors has been associated with chronic intoxications, while acute intoxication to $KBrO_3$ in humans can lead to thrombocytopenia, neuropathological disorders, and renal failure **(Shanmugavel *et al.,* 2020).** lipid peroxidation (MDA), reactive oxygen species (ROS), and 8-hydroxyguanosine (8-OH-

dG) modification production in renal DNA have been implicated in the nephrotoxic effects of $KBrO_3$. In humans and animals, the cellular antioxidative defense capacity is substantially outstripped by the oxidative stress induced by $KBrO_3$, leading to substantial nephrontoxicity plus carcinogenicity in experimental animals (**Piko *et al*., 2023)**.

Hibiscus sabdariffa L., (HS) a tropical species, is affectionately referred to as Roselle. Its native habitats are India and Malaysia. It is widely cultivated in Southeast Asia, Central and West Africa, and other tropical and subtropical regions. It has many names as Jamaica (Spanish), crimson sorrel (English), or karkadeh (Arabic) **(Thiagarajah *et al.,* 2019).** The leaves are underutilized in comparison to the blossoms, despite being the most extensive component of the roselle plants. The primary subclasses of flavonoids in leaves include rutin, quercetin, and kaempferol, as well as their derivatives **(Lyu *et al.,* 2020).** Furthermore, protocatechuic acid, chlorogenic acid, crypto chlorogenic acid, and sitosterol-β-D-galactoside have been identified in the leaves of roselle (H. sabdariffa L.) **(Wang *et al*., 2014**; **Torres *et al*., 2020**). Roselle leaves possess a substantially elevated concentration of polyphenolic compounds, including chlorogenic acid, quercetin, and kaempferol, which are related to their antihypertensive, anti-hyperlipidemic, anti-inflammatory, antimicrobial, diuretic, uricosuric, and anemia-treating properties (**Zhen *et al*., 2016; Riaz and Chopra, 2018).** It also, as fresh or dried, has a history of traditional uses in many countries as a health drink or in foods as hot and cold beverages, food coloring, jellied confections, jam, chocolates, ice cream, puddings, flavoring agents, and cake (**Edo *et al.,* 2023**). Furthermore, the presence of anthocyanins in roselle leaves is crucial for the oxidative stress response, as they can eliminate ROS (**Shen *et al.,* 2016; Almajid *et al.,* 2023).** The anthocyanins' anti-inflammatory potential has also been reported through the reduction of inflammatory mediator levels (**Hidayah, 2019).**

Tamarind (*Tamarindus indica L*.) is located in Africa, Asia, and America is a long-lived

evergreen tree that is indigenous to tropical and subtropical vegetation is the tamarind (**Zhang et al., 2024**). Soft, thick, and blackish brown, the fruit pulp is acidic and has a sour-to-sweet flavor. It is accompanied by tough seeds. The seeds are used to facilitate germination and they are glossy, firm, and reddish or purplish brown in hue (**Hemalatha and Parameshwari, 2021)**. The seeds also have bioactive components and exhibit health effects **(Zhang *et al.,* 2024)**. The tree is utilized in a variety of life aspects, including food (syrups, juice concentrates, candy, ice cream, curries, pickles, and meat sauces) and pharmaceutical uses, as well as in the industries of textile, fodder, timber, and a source of fuel **(Maria *et al.,* 2011; Bagul *et al*., 2018).** The pulp comprises approximately 55% of the fruit, while the remaining 34% is seed and 11% is shell plus pod fiber. A sweet acidic flavor has been produced by the spice's presence of tartaric acid (10%) and sugar which primarily are glucose plus fructose; it has a long history of usage as a spice in many Asian cuisines (**Martins *et al.,* 2020**). Although tamarind does not have tryptophan, it does contain every essential amino acid. It also includes organic acids as 3-10 % tartaric, acetic, formic, citric, succinic, and malic acid; 87.9 g/kg protein with amino acids of leucin, alanine, phenylalanine, serine, and proline, 25-30 % invert sugars, pectin, 19,1 g/kg fat, some thiazoles as fragrant, some pyrazines, and trans-2-hexenal **(Akhtar *et al.*, 2019)**. It is rich in B-complex vitamins and contains carotenoids, vitamin C, and minerals. Also, seeds are rich in protein and oil **(Nakchat *et al.,* 2014; Chimsah *et al,* 2020).** Tamarind has various beneficial effects in food and pharmaceutical fields because of its ingredients (**Farooq *et al.,* 2022**). In rodents, seed aqueous extract has ant diabetic effect, while the fruits have laxative, antioxidant, antifungal, and antibacterial properties **(Tawfik *et al.,* 2020; Li *et al*., 2023).** Tamarind pulp is highly edible and contains a diverse array of nutrients, including vitamins, proteins, carbohydrates, free amino acids, and minerals. Fresh tamarind fruits and foliage can be consumed as vegetables (**Mansingh, *et al.,* 2021**). Therefore, consumers hold tamarind in high regard, and it is

extensively employed in the manufacture of beverages and snacks (**Zhang et al., 2024**).

This investigation set out to assess and compare the potential nephroprotective effects of water and alcoholic extracts from tamarind, roselle, and their mixer in rodents by enhancing kidney function, anti-oxidative status, and overall health in response to potassium bromate-induced nephrotoxicity.

MATERIALS AND METHODS

Materials

Plant materials:

Tamarind (*Tamarindus indica*) and Roselle (*Hibiscus sabdariffa L.)* were designated by the Agriculture Crops Department of the Agriculture Faculty at Menoufia University. These plants were acquired from an herbalist in Shebin El-Kom City, Governorate of Menoufia, Egypt.

Animals

Our study obtained 48 adult male albino rats, each weighing 150±10 g, from the Research Institute of Ophthalmology, Animal House Department in Giza, Egypt, for this investigation, which was approved by the Institutional Animal Ethics Committee of Menoufia University. (Reg. No, MUFHE /F/NFS/26/24).

Chemical kits and potassium bromate ($KBrO_3$)

potassium bromates ($KBrO_3$ white crystals, molecular weight: 167 and code: L26221) had been acquired from Cairo, Egypt's El-Gomhoria Company for Trading Medical Instruments, Chemicals, and Drugs. Biochemical examination tools were obtained from SIGMA (USA), which is situated in Cairo, Egypt.

Methods

Determination of total phenols

By employing the subsequent methodology, the total phenols in both aqueous and alcoholic extracts were ascertained using the **Singleton and Rossi (1965)** technique and reagent of Folin coculture.

Preparation of roselle and tamarind extracts

The extracts of whole tamarind (Tamarindus indica) and roselle (Hibiscus sabdariffa) on an alcoholic or aqueous basis were produced by immersing 200 g of the respective plant in 1 L of purified water or 70% ethanol alcohol for 10-12 hours. The mélange was subsequently filtered

using the Whatman No. 1 filter (Maidstone, UK). Model RE52A Rotary Evaporator (Wincom Company Ltd., Changsha, Hunan, China) was employed to condense the filtrate to 8% of its original volume at 55ºC. In an oven at a temperature of 40ºC, the concentrated filtrate was desiccated (**Moreno *et al*., 2006)**.

Nephrotoxicity induction

Healthy Male albino rat was given orally for 4 weeks twice a week with 20 mg $KBrO_3$/kg according to body weight (**Khan *et al.,* 2012).**

Experimental animals

Before the experiments commenced, in wire enclosures, forty-eight healthy adult male albino rats, each weighing (150±10) g, were bred and kept in a laboratory that was equipped with a well-functioning ventilation system and maintained under hygienic conditions for one week as an adaptation period. The animals were habituated to the basal diet that contained maize starch (69.5%), barn (5%), casein (10%), corn oil (10%), vitamin mixture (1%), salt mixture (4%), methionine (0.3%), and choline chloride (0.2%) (with some modification according to **Reeves *et al.,* (1993)**. Specialized non-scattering feeding containers were employed to administer diets to rodents to prevent feed loss and contamination. Inverted bottles were suspended to one side of the cage, while glass tubes were used to furnish water to the rats by projecting through the wire cage. A daily monitoring of the passages was done.

Experimental design

The research was once conducted in Animal House at the Department of Nutrition and Food Science, Faculty of Home Economics, Menoufia University, Menoufia Governate, Egypt. Randomly, the rats were classified into eight studied groups as 6 rats of each. The rats were illustrated as the next: Group (1) fed on a basic diet as a negative control group, group (2) fed a basic diet and received potassium bromate ($KBrO_3$) intragastric orally twice a week for four weeks as a positive control group, Groups (3, 4, 5, 6, 7 and 8): rats orally received each of KBrO3 at (20 mg/kg body weight; aqueous) twice a week and simultaneously received roselle aqueous extract, roselle alcoholic

extract, tamarind aqueous extract, tamarind alcoholic extract, mixture aqueous extract and mixture alcoholic extract respectively at 40 mg/kg body weight daily for four weeks as an experimental period. Many searches used Tamarind and roselle extracts at several doses and durations for different purposes as **Dey *et al.,* (2011)** used 25/kg b.wt. (low), 50 mg/ kg b.wt. (medium) and 100 mg/ kg b.wt. (high) doses of tamarind extract and pursued its effects for 14 weeks, so the dose of this study based on moderate dose and duration to detect and compare the reno-protective effects of water and alcoholic extracts of tamarind or roselle and their mixer on potassium bromate- induced nephrotoxic rats.

Collection of samples

After the completion of the experiment, samples of blood were collected from the aorta in dry, clean centrifuge tubes plus left to clot after fasting overnight and for 2 hours for water. The centrifuge for 10 minutes at 4000 rounds /min. To separate sera was used. The serum was stored at –20ºC in polypropylene vials until analysis **(Schemer, 1967).** Also, kidney tissues were dissected quickly on ice for biochemical assays.

The 24-hour urine for each rat was collected at the end of the study period end. Rats were given their standard diet and water. The urine samples were collected and centrifuged to remove particles (**Jin *et al.,* 1999**).

Biochemical assays

Kidney functions

Serum urea, uric acid, and creatinine were measured according to **Patton and Crouch (1977); Fossati *et al*., (1980); and Murray (1984)** respectively.

The urine samples were collected, and their volume was measured by the graduated cylinder. Urine samples were analyzed qualitatively using urinalysis reagent strips to determine protein content, creatinine, and uric acid since clearance of creatinine and uric acid (ml/min) was calculated as a concentration in urine × urine volume (ml/min) /Concentration in serum as described previously (**Fischer et al., 2000).**

Liver functions

Methods of **Henry (1974); Young *et al.,* (1975) and Tietz *et al.,* (1983)** respectively, were used to estimate serum liver enzyme Aspartate aminotransferase (AST),

alkaline phosphatase (ALP), and alanine aminotransferase (ALT). The methods of **Spencer and Price (1977); Srivastava et al., (2002); Varley et al., (1988)** in order were used to evaluate other liver functions such as albumin, globulin, and total protein plus calculated albumin/globulin ratio (A/G ratio).

Serum lipid analysis

According to the methods of **Allain (1974), Fossati and Prencipe (1982), and Lopez (1977)** respectively, total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol HDL-c) were measured. While VLDL-c (very low-density lipoproteins) and LDL-c were calculated according to the method of **Friedwald *et al.*, (1972**) as the following: VLDL-c (mg/dl) = TG/5 and LDL-c (mg/dl) = (Total cholesterol – (HDL-c +VLDL-c).

The calculation of the atherogenic index was done according to **Hosny *et al.* (2024)** since the (AC) atherogenic coefficient also known as (AI) atherogenic index was obtained by dividing non-HDL-C by HDL-C = (TC - HDL C) / HDL C.

Renal antioxidants enzymes, MDA, and 8-OH-dG

Renal tissues levels of reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), malondialdehyde (MDA) and 8-Hydroxydeoxyguanosine (8-OH-dG) were detected according to the methods of **Moron et al., (1979); Sun *et al*., (1988); Aebi, (1984); Ohkawa *et al*., (1979) and Yin *et al*., (1995)** respectively.

Statistical analysis

SPSS program "Statistic Program Sigmastat, Statistical Soft-Ware, SAS Institute, Cary, NC" was utilized to assess the data, and the findings were given as means ± SD, followed by the variance analysis test, which was conducted using the range test of Duncan's multiple to assess various treatments effects and a one-way ANOVA was executed. To find differentiating factors among the categories, a $p \leq 0.05$ significance threshold was employed **(Snedecor and Cochran, 1967).**

RESULTS AND DISCUSSION

The total phenols content for different extracts of roselle, tamarind, and their mixture are

shown in **table (1)**. The total phenol content differed according to the method of extract and the plant's type. The alcoholic extract gave a high total phenols content in general as compared with aqueous extract. Both alcoholic and aqueous tamarind extracts were higher in total phenols content than plant mixture and roselle extracts. By descending arrangement, alcoholic tamarind being the top, then alcoholic mix and aqueous tamarind, followed by alcoholic roselle, alcoholic mix, and aqueous roselle being least phenols content.

From the obtained results, it was observed that the type of the plant and the methods of extract had a high effect on the content of the total phenols, and these findings were confirmed by studies by **Maleki *et al.,* (2019**) results who reported that roselle contained a high amount of total phenols, which was 23.77 ± 0.25 mg GAE / g, while **Bayoï *et al.(*2021)** reported that total phenols of leaf extracts of tamarind were varied about 6.14 mg GAE/g to 17.84 mg GAE/g. Phytochemical analysis of roselle has recognized secondary metabolites as flavonoids, phenolic acids, anthocyanidins, phytosterols, and organic acids (**Kamyab et al., 2022**). Chemical analysis by **Rana and Sharma (2018)** revealed that tamarind showed a higher amount of carbohydrates in seed and pulp with significance difference. In addition to the phytochemicals screening that showed the existence of flavonoids plus tannins in pulp but saponins in seeds which support the plant's traditional applications in the treatment of a variety of illnesses, whereas glycosides and alkaloids demonstrated a negative reaction. Also, **Farooq et al., (2022)** showed the existence of high flavonoid and phenolic content of tamarind which is related to its antioxidant and medicinal effects.

At the same time, the findings of this investigation conform with those of other investigations that have looked at solvent-connected phenolic extraction as **Alara *et al.,* (2021)** found that extraction technique affects the rate at which phenolic compounds are recovered from plants, so the appropriate extraction is crucial to recover the desired phenolic compounds. **Radzali *et al*., (2020)** discovered that 70% ethanol, an alcoholic co-solvent, was effective in improving

the quality of the plant's extraction and produced a comparatively clean extract that prevents oxidation, which degrades phenolic compounds, and this may relate to the contents of nonphenolic compounds as carbohydrates in the water extract **(Shi *et al*., 2022).** This may also be due to the potential creation of a phenolic complex with additional phenol groups of the extracts that are soluble in organic solvents. It is evident from this variation in results that the extracted phenolic compounds are influenced by the solvents' varying polarity **(Robards,2003)**. Also, **Ashfaq *et al*., (2021)** found that non-polar liquids work stronger than polar liquids such as water for phenolic compounds extraction.

The impact of roselle, tamarind, and their mixed extracts on serum kidney function and protein fraction of nephrotoxic rats are proven in **Table (2)**. When rats were given potassium bromate, their serum levels of renal function indicators such as creatinine, uric acid, and urea increased significantly in the positive control group as found in Table (2) compared to a healthy one. Also, the potassium bromate group had significant decreases in values of total protein, albumin, and albumin/globulin ratio related to normal values. There were no significant changes between different groups for globulin levels.

The current findings were consistent with **Spassova *et al.* (2015)** who documented that potassium bromate ($KBrO_3$), an oxidizing factor that is usually used as a food additive and in cosmetic products plus it is a tap water pollutant, has been attributed to developing of various organs damage as kidney. The toxicity of the kidney which is named nephrotoxicity due to $KBrO_3$ has been related to its capability to excite the manufacture of lipid peroxidation, ROS (reactive oxygen species), and 8-OH-dG (8-hydroxyguanosine) modifications into renal DNA and greatly surpasses the antioxidant system ability of cells to defend against free radicals, causing significant nephrotoxicity in both people and animals by significant increases in creatinine, urea and uric acid as detected by several studies as **Khan *et al.*, (2012); Ali *et al.*, (2018).** Numerous researchers found that $KBrO_3$ caused renal

abnormalities in a range of animal strains and species at varying dosages. **Khan *et al*., (2012)** reported that $KBrO_3$ administered orally twice weekly for 28 days at a dose of 20 mg/kg in male Sprague-Dawley rats produced severe renal impairments to creatinine and urea elevation plus a reduction in albumin and total protein values similar that found in this work. **Ennulat and Adler (2015)** indicated the previously proposed mechanism of kidney injury through free radical production and decreased renal markers such as albumin and total protein.

Conversely, the treats with alcoholic and aqueous tamarind as well as their mixture resulted in a significant reversal and eventual control of this detrimental trend in serum biomarkers for renal function. Although the biomarker levels of renal function were improved, no significant mean values for kidney functions (creatinine, urea, and uric acid levels) between roselle extracts and the positive control group were detected which may need a higher dose or duration to achieve a significant effect. From the same table, there is no significant between alcoholic tamarind extract and the two types of mixture extracts, being the best effects reaching insignificant levels in normal rats.

Also, compared to the positive control group, all renal toxic rodents fed on various extracts detected insignificant total protein levels from normal rats. Tamarind, mixtures, and aqueous roselle extracts showed high albumin levels with insignificant changes from the -ve control group, while the albumin/globulin ratio for tamarind and mixtures extracts only reached normal ratio without significant differences between alcoholic and aqueous extracts for each type. The group of nephrotoxic rats who acquired tamarind and mix extracts had the highest effects in total protein and albumin levels with non-significant changes either from each other or compared to the (-ve) control group.

Feeding rats on the different studied extracts have been reported to possess nephron-protective that occurred by potassium bromate and these findings were corroborated by **Ellis *et al., (*2022)** who revealed that roselle extract effect due to their

polyphenol contents and the other bioactive components with antioxidant effects, as catechin, protocatechuic acid, and epigallocatechin gallate. They can scavenge dangerous free radicals along generate more antioxidants to stop oxidative damage to cells. Also, it contained anthocyanins that showed strong antioxidant action in a liposomal system (**Manzano-Pech *et al.,* 2022; Anadozie *et al*.,2023).**

Morales-Luna *et al.,* (2019) found that roselle health effects through its antioxidant mechanism due to containing cyanidin 3-O-sambu-bioside and delphinidin 3-O-sambubioside as the main phenolic components, followed by hydroxycoumarin, chlorogenic acid, gallic acid, catechin, and epicatechin since hydroxy citric acid and hibiscus acid are considered as two major organic acids at the water and methanolic extracts. Also, dietary included roselle red dye (with anthocyanin content of 121.5 mg Cyanidin-3-rutinoside equivalent/100 g) at 0.5% and 1% for 20 days showed nephroprotective effect against an intraperitoneal single dose of cisplatin (7 mg/kg b.w) caused nephrotoxicity plus oxidative stresses in rodents as investigated by **Ademiluyi *et al.,* (2013)**; **Okoko and Oruambo (2008)** showed that roselle extract by 200 and 300 mg/ kg b.w for 5 days modulated cisplatin-caused renal and liver injury in rodents which can restore markers near to control levels as dose-dependent.

Prasongwatana *et al.,* (2008) found that consuming a cup twice daily for linked 15 days prepared from 1.5-gram of dried roselle calyx increased the excretion of urinary uric acid and may help in hyperuricemia however didn't lower serum uric acid at this dose. **Dehkhoda *et al.,* (2024)** found that roselle extract as a 350 mg pill twice a day for 3 months showed encouraging outcomes in lowering hypertension plus enhancing lipid profiles for individuals with chronic renal impairment since there is a reciprocal association between hypertension and chronic kidney disease with each factor influencing the other's severity and progression. And discussed that roselle utilization has positive impacts, including anti-hypertensive impacts, enhanced endothelial and kidney functions, diuretic activity, along anti-

hyperlipidemic impacts, attributing to the anti-inflammatory and antioxidant activities of its bioactive compounds that promote the production of endogenous antioxidant and anti-inflammatory reno-protective particles, such α-1-microglobulin and α-1-acid glycoprotein, exhibiting their physiological functions as anti-inflammatory and immune-regulatory. In another study, twice daily intake of 425 mg of roselle pill (hydroalcoholic extract of flowers) for 8 weeks markedly lowered systolic blood pressure along with kidney indicators of creatinine and urea, plus urine creatinine and albumin in diabetic nephropathy patients (**Mohammadi et al., 2021**). Moreover, **Ajani et al., (2021)** found that 200 and 500 mg/kg doses of roselle aqueous extract for modulate kidney dysfunction plus cardiovascular illness risk related to streptozotocin caused diabetes in rats. A similar study by **Hidayah (2019)** found that roselle ameliorates diabetic nephropathy via lowering ROS (reactive oxygen species), and lipid along with protein oxidation, plus decreasing renal NADPH oxidase expression and NF-κB activation, improved renal nitric oxide expression, and moderating antioxidant enzymes actions as CAT, SOD, and GSH-Px in each plasma and kidney.

On the other hand, it's worth mentioning that although roselle is frequently consumption through worldwide and is seemingly counted safe (**Edo *et al.,* 2023**) since it is described by an extremely low level of toxicity by LD50 in rats of its calyx extract being above 5000 mg/kg (**Ali *et al.,* 2005**), few statements refer some adverse impacts to it since the histopathological results by **Nwachukwu *et al.,* (2009)** showed that high dose of aqueous extract of roselle at 80 and 160 mg/kg body weight for long period (12 weeks) hurt the kidney and didn't effect on the liver, while lower doses or consume periods were safe. Also, **Fakeye *et al.,* (2009)** found that 2000 mg/kg oral dose administration of water plus alcohol extracts for 3 months of dried roselle preceded the animal's death by serious weight loss companies with diarrhea, while 300 mg/kg increased food intake. And no significant histo-pathological changes were observed.

Additionally, treatment results using tamarind extracts agree with Muzaffar and Kumar (2017), who documented that most of the phytochemicals found in tamarind aid in kidney detoxification. The amount of potassium in tamarind is sufficient to remove the harmful substances that accumulate in the renal. **Tawfik *et al.* (2020)** found that tamarind seed extract of 230mg/each rat once daily for 6 weeks before irradiation significantly abolished γ-rays-induced nephrotoxicity and it can act as a strong anti-inflammatory and antioxidant medication to stop or minimize the harmful impacts of γ-rays (8Gy). Also, bioactive components documented in tamarind extract as flavonoids, phenolics, carotenoids, and anthocyanins are biologically significant in the prevention and/or treatment of numerous illnesses such as diabetes, obesity, atherosclerosis, cancer, and kidney diseases through its scavenging free radicals and antioxidant activity (**Li *et al*., 2023).** Tartaric acid (TA), as a main compound of common fruits like tamarind, showed antioxidant activity plus prevents kidney stone formation; however, TA's pharmacological actions do not imply that it should be taken without supervision and it has a daily limit of 30 mg/kg depending on body weight since it has hazardous effects that lead to teeth erosion and acidosis (**Jantwal *et al.,* 2022**). Also, supplementation with tamarind fruit pulp extract at 200 mg kg^{-1} based on body weight for 3 months alleviated the adverse effects in kidney and liver of sodium fluoride exposed rats as 2% in drinking water by enhancing antioxidant status as found by **Gupta *et al.,* (2013)**. Moreover, co-therapy with gentamicin and daily tamarind aqueous-ethanol extract at 200 mg/kg significantly improved renal structure and function by improving serum creatinine, urea, and uric acid plus urinary markers **(Ullah *et al.,* 2014)**. Tamarind could be categorized as virtually nontoxic plus it seemed safe according to the World Health Organization (WHO) and the Organization of Economic and Cultural Development (OECD) since the LD50 of the extract of tamarind pulp is more than 5000 mg/kg bw (**Abubakar *et al.,* 2010)**, also following the delivery of 5000 mg/kg bw of it, there was no deaths as detected by

Lim *et al.*, (2013). Moreover, **Iskandar *et al.*, (2017)** exhibited that long-term (6 months) utilization of water extract of tamarind pulp was well tolerated and generally safe at 1000 mg/kg bw, being the highest tested dose.

The impact of roselle, tamarind, and their mixed extracts on urinary markers of nephrotoxic rats are shown in **Table (3**). related to the control group, potassium bromates caused a significant elevate in urine volume and urine protein contents. The negative control group had the higher creatinine and uric acid clearance while the positive control group recorded the lower mean value. Many studies showed the nephrotoxicity effect of potassium bromate as dose-dependent, evident by several measures of renal structural, functional indices, and toxicity biomarkers. **Khan *et al*., (2012)** showed that serum levels of creatinine and urea significantly increased whereas creatinine clearance was reduced by potassium bromate orally consumption twice a week for 4 weeks at 20 mg/kg bw. Also, the results by **Ali et al., (2018)** indicated that creatinine clearance was dose-dependently diminished by potassium bromate intake at 5, 15, 45, and 135 mg/kg/day for 28 days, and urine output significantly increased in the highest potassium bromate dose.

The clearance is known as the plasma volume that may be entirely removed from a particular substance in a time unit, and it is based on indicators of kidney function. Creatinine clearance could be considered an estimate of the glomerular filtration rate (GFR) that is used in the classification of renal disease according to the fall degree (**Ferguson and Waikar, 2012**). Also, hyperuricemia can be caused as the result of uric acid clearance reduction, and reduced blood uric acid levels can occur in different ways as enhancing uric acid clearance **(Ronco and Rodeghiero, 2005)**.

On the other hand, in comparison with the control + group, there was a substantial drop in the urine protein contents in potassium bromate tread groups with alcoholic and aqueous extracts of tamarind, roselle, and their mixture since the best reductions recorded for alcoholic tamarind extraction and both of mixture extraction which didn't significantly difference from each

other. No significant changes were detected in the case of urine volume. Also, the rise in creatinine and uric acid clearance was significantly detected for tamarind and mixture extracts groups since no significant was detected between the positive control group and both roselle extracts. The highest effect on each creatinine and uric acid clearance was detected in the group treated with alcoholic tamarind extract reaching a nonsignificant change from the negative control group, then aqueous tamarin extract and both mixture extracts which didn't significantly differ from each other. These results come in harmony with that finding by some searches as **Yang *et al.,* (2013)** who found that roselle polyphenol extract prevents diabetic nephropathy and significantly improves albuminuria and creatinine clearance. Also, roselle is included as a diuretic herbal medicine as reported by **Wright *et al.,* (2007)**. Moreover, **Ullah *et al.,* (2014)** showed that daily tamarind aqueous-ethanol extract at 200 mg/kg co-administration with gentamicin had significantly improved renal structure and different kidney function biomarkers as improving urinary markers of creatinine clearance and urinary volume and decreased protein excretion, plus improving blood biomarkers. In addition, **Kaundinnyayana *et al.,* (2015)** found that tamarind fruit pulp water extract at dosages of 300, 600, and 1200 mg/kg has diuretic activity by significant effect for 1200 mg/kg dose in Wistar rats. While the differences in urinary elements next to intake tamarind product that is ready to eat and include 65% moisture 10 g for 3 weeks by 30 individuals from an endemic area for fluoride showed no change in urinary volume, but urine pH and fluoride excretion significantly increased, while urine calcium and copper excretion significantly decreased as found by **Khandare *et al.,* (2004)**.

It is worth mentioning the found by **Prasongwatana *et al.,* (2008)** that a cup twice daily for linked 15 days prepared from 1.5 grams of dried roselle calyx by subjects increased uric acid clearance and urinary uric acid excretion that is recognized to be a risk for urinary stone formation as calcium oxalate stone without any evidence of antilithiatic effect although this uricosuric effects

may be help for treating hyperuricemia of gout illness. On the other hand, **Woottisin et al., (2011)** found that consuming 3.5 mg of roselle daily by rats due to higher oxalate urinary excretion and lower renal tissue calcium content that reduced calcium crystal accumulation in the renal, and such antilithic action could be linked to lowered oxalate holding in the renal and increased excretion via urine. Moreover, a study by **Curhan and Taylor (2008)** does not encourage the commonly accepted belief that elevated excretion of uric acid in the urine raises the chance of formation of calcium oxalate stones. Furthermore, there is a need to reevaluate the existing definitions of urine normal factors.

Anyway, the potential risk of stone formation should be considered, and this risk or potentially harmful effects can be limited by several suggestions as increasing water intake, decreasing sequent consumption duration by taking rest periods as 2 or 3 days between all treated periods, and avoiding consuming high doses. Also, further searches are needed in these respects.

The impact of tamarind, roselle, and their mixed extracts on renal antioxidant status, lipid peroxidation, and 8-OH-dG, an oxidative DNA product in nephrotoxicity rats are presented in **Table (4)**. Potassium bromate was related to exciting renal oxidative injury as manifested by the increasing of malonaldehyde and 8-hydroxydeoxyguanosine while, renal antioxidants were significantly decreased "SOD, CAT, and GSH". These observations might be caused by the nephrotoxic impact of $KBrO_3$, which can trigger kidney oxidative stress **(Ali *et al*., 2018**). The renal is sensitive to oxidative stress due to its low levels of antioxidant defense mechanisms as antioxidant enzymes (**Kamel *et al.,* 2023)**. **Li *et al.,* (2020)** showed that the unequal generation and consumption of ROS (reactive oxygen species) results in oxidative stress, which damages intracellular macromolecules (like lipids, proteins, and DNA) irreversibly and speeds up the course of numerous illnesses, including nephritis, cardiovascular , diabetes, cancer, and neurological disorders. $KBrO_3$, which is a by-product of disinfected water by

ozonation or a food additive, at different doses either as a single dose injection or administration in drinking water for 4 weeks induced DNA oxidation described by significant elevating in 8-oxo deoxyguanosine (8-oxodG) which may happen due to lipid peroxidation and over 250 ppm $KBrO_3$ in drinking water able to cause renal carcinogenic impact via oxidative stress as found by (**Umemura *et al.,* 2004)**. Likewise, **Akomolafe *et al*., (2021)** revealed that the lipid peroxidation of rats renal is increased by $KBrO_3$, which also decreases glutathione peroxidase (Gpx) activity and increases the production of free radicals such as superoxide anion, NO (nitric oxide anion), plus ONOO– (peroxynitrite anion). They demonstrated a significant lower in the GSH level and also CAT, SOD, and GPX activities for $KBrO_3$ administered group as compared to the normal group, which is in line with this study's results. Also, **Khan *et al*., (2012)** stated that the decrease in antioxidant responses considered an interest in the renal toxicity with $KBrO_3$.

In contrast, the cotreated group with potassium bromate and different examined extractions showed a reduction in the expression of malonaldehyde and 8-hydroxydeoxyguanosine whereas caused increases in antioxidants except for the resole extracts which recorded mean values nearly to a positive control group with nonsignificant changes. The highest effect significantly was shown in both mixture extracts followed by the effect of alcoholic tamarind extract compared with other treated groups and the positive control group.

The current findings stated that oral administration of tamarind or its mixture with roselle extractions along with $KBrO_3$ through the experimental period significantly decreased the renal levels of 8-OH-dG and MDA, plus elevated the renal activities of CAT, SOD, and GSH levels significantly compared with $KBrO_3$-administration group. According to searches on the antioxidant activities of roselle ethanolic extract, total antioxidant activities exhibited a rise in concentricity and then absorbance rise (**Subhaswaraj *et al.,* 2017**). Roselle extract contains anthocyanin which can scavenge free radicals by its antioxidant properties **(Nurnasari and**

Khuluq 2017). Anthocyanins are members of the flavonoid group which has antioxidant properties, since anthocyanin's conjugated double bond structure aids in the capture of free radicals. In addition to anthocyanins, roselle extract contains beta-carotene, vitamin C, flavonoids, and polyphenols since chlorogenic acid, the most prevalent and useful polyphenol, is well known for its antioxidant activities **(Edo *et al.,* 2023)**. **(Ulialbab *et al.,* 2015)** reported that it is capable of roselle extract to lower malondialdehyde levels. Further, **Zuraida *et al.* (2015)** found that extract of roselle can lower MDA and raise the catalase enzyme value of carbon tetrachloride exposed rats, and **Pramita (2014)** reported that roselle extract can raise SOD and lower MDA values in the eyes of rats exposed to 300 rad gamma radiation. **Okoko and Oruambo (2008)** showed that roselle extract by 200 plus 300 mg/ kg b.w. for 5 days modulated cisplatin-caused oxidative renal along with liver tissue injury in rats characterized by significant decreases in catalase and reduced glutathione which can restore markers near to control levels as dose-dependent. Moreover, oral intake of alcoholic roselle extract for 45 days at 250 mg/ kg b.w reduced lipid peroxidation of kidney and liver tissues accompanied by elevated antioxidant levels in hyper-ammonemia rats caused by 100 mg/kg b.w. ammonium chloride daily injections intraperitoneally as found by **Essa *et al.,* (2006)**. Accordance to **Lemmens *et al.* (2014)**, When flavonoid molecules undergo oxidation, a metabolite component is produced that has the potential to harm the body's natural antioxidant glutathione GS H). It is believed that endogenous antioxidant damage results in a reduction in intracellular antioxidant activity, which in turn causes ROS (reactive oxygen spec ies) to interact with kidney cell molecules, continuing the lipid peroxidation procedure and producing a high MDA (**Alyani *et al.,* 2021**).

Certain study results of tamarind extract or with roselle mixture are harmonic with the findings of **Zhou *et al.*, (2021)** who appeared that numerous phytochemicals found in tamarind, primarily flavonoids, polyphe-nols, and polysaccharides, can be used to reduce oxidative stress,

raise GSH levels, and boost the production of the antioxidant enzymes of SOD and CAT. Also, it has been reported that the ability of plant extracts with polyphenol components to donate electrons or hydrogen atoms and neutralize free radicals is what gives them their antioxidant properties. Tamarind fruit pulp extract (70% ethanolic) displayed valuable radical scavenging action in vitro plus diminished serum lipid peroxidation with enhanced anti-oxidant defense in regards to CAT, SOD, and Gpx (**Martinello *et al*., 2006; Sadi *et al*., 2021)**. Also, supplementation with tamarind pulp extract at 200 mg kg^{-1} according to body weight for 3 months alleviated the adverse effects in the kidney and liver of sodium fluoride-exposed rats as 2% in drinking water by enhancing antioxidant status as found by **Gupta *et al.,* (2013)**. Moreover, tamarind seed extract before irradiation by γ-rays (8Gy) can significantly abolish alleviation in kidney CAT and GPx activities and decreased GSH values plus limited inflammatory and structure damage as evaluated by **Tawfik *et al.,* (2020)**. **Atawodi *et al.* (2013)** examined the in vivo antioxidant activity of the alcoholic extract of tamarind in various parts since the extracts exhibited natural antioxidant activities, and the peel compared to other tamarind parts provided the most anti-oxidation active. Additionally in vitro study by **Farooq *et al.,* (2022)** showed that tamarind is rich in flavonoids and phenols plus exhibited antioxidant activity through various techniques such as DPPH (2,2-diphenyl-1-picrylhydrazyl), ABTS (Thiobarbituric acid reactive Substances), metal chelation activity and lipid peroxidation method TBARS (2,2-Azino-Bis-3-Ethylbenzothiazoline-6-Sulfonic Acid) assays, so it has various beneficial effects in food and pharmaceutical fields. **Zhang *et al.,* (2024)** indicated the need for further studies about whether tamarind polysaccharides have a role in its antioxidant activity that is extremely reliant on their solubility, molecular weight, sugar ring structures, presence of negative or positive charged groups, protein moieties plus covalently linked phenolic components.

The impacts of water and alcoholic extracts of tamarind, roselle, and their mixture on the

serum mean values of triglycerides, total cholesterol, and cholesterol fractions plus atherogenic index in nephrotoxic rats were demonstrated in **Table (5).** The acquired results of the potassium bromate group showed a bad lipids profile characterized by a significant increase in TG (triglycerides), TC (total cholesterol), LDL-C (low-density lipoprotein cholesterol), VLDL-C (very low-density lipoprotein cholesterol) plus atherogenic index AI (TC/HDL-C) while high-density lipoprotein cholesterol (HDL-C) was greatly reduced in comparison with the negative control group.

Many studies showed that potassium bromate, which is still used as food additives in bakery processing and found as byproduct in disinfected water by ozonation, at various doses and duration induced oxidative stress related to dyslipidemia and pathogenesis of many chronic diseases as atherosclerosis and hypertension such as **Oladele *et al.,* (2020)** who found that $KBrO_3$ change lipid profile by a noticeable lower in HDL-C plus elevates in total cholesterol, LDL-Cholesterol, and coronary heart disease risk ratio (TC/HDLC) compared to normal group. Also, Numerous studies have shown that while greater HDL is related to a decreased incidence of cardiovascular problems, rising LDL is linked to a higher risk of atherosclerosis. As the current investigation found, the atherogenic index, which could be employed to predict the danger of developing cardiovascular diseases, increased as the values of serum HDL reduced due to the $KBrO_3$ administration (**Ugwu *et al.,* 2022).** There was a well-known, relationship between cardiovascular disorders such as atherosclerosis and hypertension and chronic kidney diseases (CKD), contributing to each other's development and severity as explained by **Dehkhoda *et al.,* (2024)**. So, the increasing burden of CKD will be lessened by controlling cardiovascular disease (**Francis *et al.,* 2024**).

All roselle, tamarind, and their mixture extracts were associated with lower serum triglycerides, total cholesterol, AI, and cholesterol fractions except HDL-c which increased as compared with the nephrotoxic group. There were no significant changes between all tested extracts

regarding the improvements of TG, VLDL-C, and AI which reaching to insignificant changes from levels of normal rats. The TC and LDL-C results showed significant reductions from the positive control group for all extracts by best effect for alcoholic extracts of mix and tamarind, and it is worth observing that all TC levels for all extracts reaching nonsignificant changes from TC level of normal rats while LDL-C of mix alcoholic extract only reaching to normal level. HDL-C results showed the best elevations for both extracts of roselle and mixed extracts. These results indicated that mixing extracts especially alcoholic ones as the best effects in general towards improving lipids profile and atherogenic index.

These findings concur with **Prasomthong *et al., (*2022)** who documented that the roselle calyces and leaves that are rich in polyphenol and flavanol- possess powerful antioxidant and antihyperlipidemic qualities as examined by their in vitro lipid peroxidation inhibitory action and in vivo impacts on cholesterol-induced hyperlipidemia. Also, **Ajiboye *et al.,* (2016); Edo *et al.,* (2023)** found that roselle demonstrated a significant lower in serum TC, LDL-c, VLDL-c, TG plus atherogenic index levels along with a rise of serum HDL-c levels. Moreover, **Dehkhoda *et al.,* (2024)** showed that extract of roselle as 350 mg pill twice a day for 3 months exhibited encouraging outcomes in lowering blood pressure plus improvement of lipids-profile for patients of chronic renal illness since the rich anthocyanins content of roselle related to these effects, so it has beneficial effects related to preventing the progression of CKD.

The findings of this study come in harmony with those found by **Martinello *et al.,* (2006)** since tamarind extract can reduce serum TG, TC, and non-HDL cholesterol addition to elevate HDL-C which inhibits the risk of atherosclerosis development with a cholesterol-fed diet, attributing by improving antioxidants defense system. **Arshad *et al*., (2019)** explained the ways of hypocholesterolemia properties of tamarind extract with a substantial increase in manifestation genes of Apo A1 (Apolipoprotein AI), LDL, and ABCG5 (ATP-binding cassette sub-family G member 5) receptor

and important inhibition the expression of HMG-CoA (3-hydroxy-3-methylglutaryl coenzyme A) reductase and levels of MTP (microsomal triglyceride transfer protein) genes; this in addition to increasing cholesterol excretion, increasing the uptake with the removal of LDL, then, induced decreased triglyceride accumulation along with inhibited cholesterol biosynthesis. **Buchholz and Melzig (2016)** discovered novel natural pancreatic lipase inhibitors by tamarind peel methanolic extract which has high anti-lipase activity. Also, tamarind seeds include phenolic substances such as phytosterols for about 590 mg/kg dry weight which are specifically beta-sitosterol known to reduce plasma lipoprotein along with cholesterol through decreasing the solubility and absorption of cholesterol across the intestinal barrier because the hydrophobicity of phytosterols allows them to interact with bile salts plus acid micelles more easily than animal cholesterol, which leads to the excretion of a larger portion of unabsorbed cholesterol, especially LDL with the faces (**Uchenna *et al.,* 2018)**. Moreover**,** the trypsin inhibitor, one of the antinutrients in tamarind seeds, is the key ingredient emphasized to lower triglycerides (**Martins et al., 2020**).

The results of **Table (6)** showed the impact of roselle, tamarind, and their mixtures as aqueous and alcoholic extracts on alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) as liver enzymes of nephrotoxic rats. It was observed that the greatest liver enzyme ranges were recorded for the $KBrO_3$ administration group. It was reported by many previous searches that $KBrO_3$ as a dose plus time-dependent induces hepatotoxicity by oxidative stress, lipid peroxidase, oxidative DNA damage, and minimum anti-oxidants defense system as **Al-Mareed *et al.,* (2022)**. **Radwan *et al.,* (2022)** showed liver function impairment by $KBrO_3$ characterized as elevating AST, ALT, and ALP enzymes since they are considered as most sensitive biomarkers for diagnosis of liver disorders plus toxicity by chemicals. Elevated levels of these enzymes occur as a result of hepatocellular injury which leads to leakage of the enzymes from the hepatocyte to the blood as

indicated by **Turan and Celik (2016)**.

An increase in liver enzyme levels that was noticed in the potassium bromate-treated rats was subsided after co-administration of alcoholic and aqueous tested extracts by significant improvements for tamarind and mixing different extracts compared to the positive control group; while roselle extracts may need the highest dose and/or period than that used in this study. The perfect effects for all liver enzymes detected for alcoholic extracts type of mix along with tamarind which didn't significantly change either from normality levels or each other. This indicates the hepatoprotective action of the plant extracts against bromate-induced liver damage. **Gou *et al.*, (2016)** indicated the interference between hyperlipidemia and enlarged lipids oxidation and the progression of liver impairment. So, tested extracted in this study by having anti-hyperlipidemia and anti-oxidant activities can help to prevent and/ or manage liver disorders. This comes in harmony with that found by **Ujianti *et al.*, (2023)** since roselle had a preventive impact against hepato-toxicity in rats caused by tart butyl hydroperoxide attributed to the high vitamin C and polyphenols (protocatechuic acid) contents which serves as an antioxidant. **Okoko and Oruambo (2008)** showed that roselle extract for 5 days by 200 plus 300 mg/ kg according to body weight-modulated cisplatin-caused oxidative renal and liver tissue injury in rats characterized by significant decreases in catalase and reduced glutathione which can restore markers near to control levels as dose-dependent. Also, oral intake of alcoholic roselle extract for 45 days at 250 mg/ kg based on body weight reduced lipids peroxidation of kidney and liver tissues accompanied with elevated anti-oxidant levels in hyperammonemia rats caused by 100 mg/kg b.wt. daily injections of ammonium chloride intraperitoneally as found by **Essa et al., (2006)**. Additionally, a study by **Amaechil *et al*., (2022)**, in which tamarind showed hepatoprotective effect by reducing AST, ALT, and ALP enzyme values in rats. Also, supplementation by tamarind pulp extract at 200 mg kg^{-1} b.wt. for 3 months alleviated the adverse effects in the kidney and liver of

sodium fluoride-exposed rats as 2% in drinking water by enhancing antioxidant status as found by **Gupta *et al.*, (2013)**.

CONCLUSION:

The results of this investigation confirmed the theory that roselle and tamarind contain phenolic components which in charge of various biological actions. The tested extracts exhibited reno-protective roles characterized by lowering serum creatinine, urea, uric acid, and urinary protein plus increasing serum albumin, total protein, and clearance of creatinine along with uric acid. The significant effects detected for tamarind and mix different extracts especially alcoholic ones, while roselle extracts may need the highest dose and/or period than that used in this study. The extracts' reno-protective action attributed to activities such as antioxidant, antihyperlipidemia, antiatherosclerosis plus inhibition renal lipids and DNA oxidation as malondialdehyde and 8-hydroxy-deoxyguanosine (8-OH-dG) results showed. Extracts also showed hepatoprotective effects. Therefore, it is necessary to enhance the use of these plants, fresh or dried, either as beverages or food supple-mentation as coloring and flavoring agents or therapeutic formulae or even in general cooking as usually used in many countries. further searches are needed to detect the ideal safe amount and usage duration. Also, potassium bromates, which are still used as food additives should be abolished.

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Table (1): The total phenol content (as gallic acid equivalent) of aqueous and alcoholic extracts of tamarind, roselle, and their mixture.

Extracts	Total phenol content (ppm) (as gallic acid equivalent) Mean ± SD
Roselle aqueous extract	**565.7^{e}± 48**
Roselle alcoholic extract	**1380.1^{c} ± 110.4**
Tamarind aqueous extract	**1645.9 ^{b}± 142.6**
Tamarind alcoholic extract	**2107.8 ^{a}± 92.4**
Mixture aqueous extract	**1105.8 ^{d}± 94.2**
Mixture alcoholic extract	**1743.95 ^{b}±146.55**

Each value as Mean ± SD (n=3)

Table (2): Impact of water and alcoholic extracts of tamarind, roselle, and their mixture at 40 mg/kg bw daily for 4 weeks on serum kidney function and protein in potassium bromates-induced nephrotoxicity rats.

Parameters Groups	Urea (mg/dl) Mean ± SD	Creatinine (mg/dl) Mean ± SD	Uric Acid (mg/dl) Mean ± SD	Total Protein (g/dl) Mean ± SD	Albumin (A) (g/dl) Mean ± SD	Globulin (G) (g/dl) Mean ± SD	A / G ratio
Control (-)	24.78^{c}±2.21	0.65^{c}±0.06	2.08^{c}±0.19	6.85^{a}±0.67	4.14^{ab}±0.39	2.71^{a}±0.26	**1.53^{ab}±0.14**
Control (+)	42.79^{a}±3.66	1.11^{a}±0.09	3.76^{a}±0.35	5.59^{b}±0.52	3.04^{d}±0.29	2.55^{a}±0.25	**1.19^{c}±0.11**
40 mg/kg RWE	38.2^{a}±2.88	1.09^{a}±0.08	3.74^{a}±0.35	6.53^{ab}±0.62	3.56^{bcd}±0.35	2.97^{a}±0.27	**1.2^{c}±0.1**
40 mg/kg RAE	39.775^{a}±3.55	1.08^{a}±0.08	3.75^{a}±0.35	6.16^{ab}±0.59	3.28^{cd}±0.31	2.88^{a}±0.25	**1.14^{c}±0.11**
40 mg/kg TWE	29.94^{b}±2.75	0.82^{b}±0.07	3.11^{b}±0.29	6.61^{ab}±0.65	3.79^{abc}±0.35	2.82^{a}±0.26	**1.34^{bc}±0.14**
40 mg/kg TAE	23.015^{c}±2.05	0.63^{c}±0.06	1.95^{c}±0.18	7.02^{a}±0.69	4.26^{a}±0.40	2.76^{a}±0.27	**1.54^{ab}±0.12**
40 mg/kg MWE	22.75^{c}±1.97	0.61^{c}±0.06	2.02^{c}±0.19	6.79^{a}±0.65	4.25^{a}±0.39	2.54^{a}±0.23	**1.67^{a}±0.15**
40 mg/kg MAE	**25.74^{bc}±1.64**	**0.69^{c}±0.03**	**2.17^{c}±0.19**	**6.97^{a}±0.12**	**4.34^{a}±0.15**	**2.63^{a}±0.22**	**1.65^{a}±0.08**

Data are expressed as mean ± standard deviation. Values within a row having different superscripts are significantly different ($p \leq 0.05$) as indicated by one-way ANOVA followed by Duncan's multiple range test ($a > b > c > d > e > f$).
RWE, roselle water extract; RAE, roselle alcoholic extract; TWE, tamarind water extract; TAE, tamarind alcoholic extract; MWE, mixture water extract; MAE, mixture alcoholic extract

Table (3): Impact of water and alcoholic extracts of tamarind, roselle, and their mixture at 40 mg/kg bw daily for 4 weeks on urine volume, urine protein, creatinine clearance, and uric acid clearance in potassium bromates induced nephrotoxicity rats.

Parameters Groups	Urine Volume (ml/24 h) Mean ± SD	Urine Protein (g/24 h) Mean ± SD	Creatinine Clearance (ml/min) Mean ± SD	Uric Acid Clearance (ml/min) Mean ± SD
Control (-)	2.55^{b}±0.24	0.0068^{e}±0.0007	0.1928^{a}±0.0192	**0.0151^{a}±0.0015**
Control (+)	3.98^{a}±0.38	0.0275^{a}±0.0025	0.0894^{c}±0.0089	**0.0042^{d}±0.0004**
40 mg/kg RWE	3.54^{a}±0.31	0.0169^{bc}±0.0016	0.0951^{c}±0.0088	**0.0047^{d}±0.00043**
40 mg/kg RAE	4.1^{a}±0.39	0.0189^{b}±0.0018	0.0908^{c}±0.0091	**0.0045^{d}±0.00045**
40 mg/kg TWE	3.87^{a}±0.34	0.0170^{bc}±0.0016	0.155^{b}±0.0144	**0.0064^{c}±0.0006**
40 mg/kg TAE	3.69^{a}±0.31	0.0151^{cd}±0.0013	0.195^{a}±0.0192	**0.0089^{b}±0.0009**
40 mg/kg MWE	3.94^{a}±0.32	0.013^{d}±0.0011	0.1661^{b}±0.0166	**0.0075^{c}±0.0008**
40 mg/kg MAE	**4.09^{a}±0.3**	**0.0144^{cd}±0.0014**	**0.1615^{b}±0.0161**	**0.0068^{c}±0.0007**

Data are expressed as mean ± standard deviation. Values within a row having different superscripts are significantly different ($p \leq 0.05$) as indicated by one-way ANOVA followed by Duncan's multiple range test (a > b > c > d > e > f).
RWE, roselle water extract; RAE, roselle alcoholic extract; TWE, tamarind water extract; TAE, tamarind alcoholic extract; MWE, mixture water extract; MAE, mixture alcoholic extract.

Table (4): Impact of water and alcoholic extracts of tamarind, roselle, and their mixture at 40 mg/kg bw daily for 4 weeks on renal antioxidant status, malondialdehyde (MDA), and 8-hydroxydeoxyguanosine (8-OH-dG, an oxidative DNA product) in potassium bromates induced nephrotoxicity rats.

Parameters Groups	CAT (Mmol/g tissue) Mean ± SD	SOD (u/g tissue) Mean ± SD	GSH (ng/g tissue) Mean ± SD	MDA (Mmol/g tissue) Mean ± SD	8-OH-dG (pg/g tissue) Mean ± SD
Control (-)	79.135^{a}±7.595	67.455^{a}±6.62	9.615^{a}±0.9252	25.475^{e}±2.415	**48.84^{d}±4.57**
Control (+)	45.405^{e}±4.23	31.12^{d}±2.97	4.25^{e}±0.3804	92.12^{a}±8.997	**139.63^{a}±12.85**
40 mg/kg RWE	47.73^{de}±4.45	33.1^{d}±2.83	4.75^{de}±0.4251	85.87^{ab}±8.39	**141.79^{a}±12.51**
40 mg/kg RAE	51.32^{cde}±4.78	36.67^{cd}±3.38	5.2^{de}±0.5003	80.99^{ab}±7.72	**139.6^{a}±11.11**
40 mg/kg TWE	57^{cd}±4.88	41.67^{c}±3.79	5.4^{cd}±0.4703	79.55^{b}±8.26	**121.13^{b}±10.46**
40 mg/kg TAE	61.47^{bc}±9.89	41.34^{c}±3.71	6.3^{c}±0.5956	59.52^{c}±5.62	**118.62^{b}±10.004**
40 mg/kg MWE	60.11^{bc}±5.37	52.435^{b}±4.99	7.713^{b}±0.6733	45.205^{d}±4.18	**73.42^{c}±6.94**
40 mg/kg MAE	**70.38^{ab}±4.08**	**60.775^{a}±3.98**	**7.565^{b}±0.4044**	**32.71^{e}±2.12**	86.925^{c}±4.44

Data are expressed as mean ± standard deviation. Values within a row having different superscripts are significantly different ($p \leq 0.05$) as indicated by one-way ANOVA followed by Duncan's multiple range test (a > b > c > d > e > f).

RWE, roselle water extract; RAE, roselle alcoholic extract; TWE, tamarind water extract; TAE, tamarind alcoholic extract; MWE, mixture water extract; MAE, mixture alcoholic extract.

CAT, catalase; SOD, superoxide dismutase; GSH, glutathione reductase; MDA, malondialdehyde; 8-OH-dG, 8-hydroxydeoxyguanosine (an oxidative DNA product).

Table (5): Impact of water and alcoholic extracts of tamarind, roselle, and their mixture at 40 mg/kg bw daily for 4 weeks on lipid profile and atherogenic index (AI) in potassium bromates induced nephrotoxicity rats.

Parameters Groups	TG (mg/dl) Mean ± SD	TC (mg/dl) Mean ± SD	HDL-C (mg/dl) Mean ± SD	LDL-C (mg/dl) Mean ± SD	VLDL-C (mg/dl) Mean ± SD	AI (TC/HDLc) Mean ± SD
Control (-)	93.85^{b} ± 7.39	114.43^{bc} ± 9.94	67.99^{a} ± 1.81	27.67^{d} ± 2.46	18.77^{b} ± 1.03	**1.64^{b} ± 0.135**
Control (+)	114^{a} ± 10.402	157.24^{a} ± 13.55	54.71^{c} ± 4.93	79.62^{a} ± 6.07	22.8^{a} ± 1.497	**2.87^{a} ± 0.251**
40 mg/kg RWE	99.88^{ab} ±9.55	127.11^{bc} ±11.01	69.06^{a} ±4.897	38.07^{c} ±2.91	19.98^{ab} ±1.61	**1.84^{b} ±0.17**
40 mg/kg RAE	103.43^{ab} ±9.61	134.35^{b} ±13.31	70.4^{a} ±5.74	44.264^{b} ±1.02	20.686^{ab} ±1.81	**1.91^{b} ±0.173**
40 mg/kg TWE	105.77^{ab} ±9.65	115.14^{bc} ±10.89	59.81^{bc} ±3.36	34.176^{c} ±1.28	21.154^{ab} ±1.935	**1.93^{b} ±0.036**
40 mg/kg TAE	107.43^{ab} ±10.11	111.82^{c} ±10.49	57.639^{bc} ±4.88	33.104^{c} ±2.28	21.486^{ab} ±1.95	**1.94^{b} ±0.18**
40 mg/kg MWE	102.48^{ab} ±9.36	123.58^{bc} ±11.29	68.63^{a} ±5.39	34.454^{c} ±2.52	20.496^{ab} ±1.931	**1.8^{b} ±0.17**
40 mg/kg MAE	**99.5^{ab} ±6.68**	**112.09^{c} ±5.82**	**64.69^{ab} ±1.21**	**27.53^{d} ±2.19**	**19.9^{ab} ±1.34**	**1.73^{b} ±0.055**

Data are expressed as mean ± standard deviation. Values within a row having different superscripts are significantly different ($p \leq 0.05$) as indicated by one-way ANOVA followed by Duncan's multiple range test (a > b > c > d > e > f).

RWE, roselle water extract; RAE, roselle alcoholic extract; TWE, tamarind water extract; TAE, tamarind alcoholic extract; MWE, mixture water extract; MAE, mixture alcoholic extract.

TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; VLDL-C, very low-density lipoprotein cholesterol; AI ((TC - HDL C) / HDL C), atherogenic index.

Table (6): Impact of water and alcoholic extracts of roselle, tamarind, and their mixture at 40 mg/kg bw daily for 4 weeks on liver enzymes in potassium bromates-induced nephrotoxicity rats.

Parameters Groups	AST (U/l) Mean ± SD	ALT (U/l) Mean ± SD	ALP (U/l) Mean ± SD
Control (-)	147.16^{c}±13.296	74.05^{d}±5.47	**178.64^{c}±17.66**
Control (+)	228.84^{a}±17.45	173.99^{a}±15.36	**294.34^{a}±28.03**
40 mg/kg RWE	219.8^{a}±21.04	166.5^{a}±6.18	**289.21^{a}±25.23**
40 mg/kg RAE	201.21^{ab}±18.97	156.55^{ab}±14.56	**259.88^{a}±23.49**
40 mg/kg TWE	185.36^{b}±18.096	141.61^{b}±12.3	**221.29^{b}±21.096**
40 mg/kg TAE	147.55^{c}±14.46	85.48^{cd}±7.63	**163.76^{c}±10.98**
40 mg/kg MWE	149.37^{c}±12.29	101.86^{c}±9.44	**220.49^{b}±21.27**
40 mg/kg MAE	**146.33^{c}±12.88**	**80.73^{d}±3.89**	**162.6^{c}±14.83**

Data are expressed as mean ± standard deviation. Values within a row having different superscripts are significantly different ($p \leq 0.05$) as indicated by one-way ANOVA followed by Duncan's multiple range test ($a > b > c > d > e > f$).
RWE, roselle water extract; RAE, roselle alcoholic extract; TWE, tamarind water extract; TAE, tamarind alcoholic extract; MWE, mixture water extract; MAE, mixture alcoholic extract.
AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase.

تأثير مستخلصات الكركديه أو التمر الهندي ومخلوطهما على سمية الكلى المستحدثة ببرومات البوتاسيوم في الجرذان

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الملخص العربي

برومات البوتاسيوم، التي لا تزال تستخدم كمضافات غذائية وتوجد كمنتج ثانوي في المياه المطهرة بالأوزون، تسبب الإجهاد التأكسدي المرتبط بالتسمم الكلوي والتسبب في العديد من الأمراض المزمنة. مصر هي واحدة من أعلى معدلات الوفيات الناجمة عن خلل في الكلى. لذا هدفت هذه الدراسة إلى مقارنة الدور الوقائي لكل من المستخلصين المائي والكحولي للكركديه والتمر الهندي وخليطهما ضد التسمم الكلوي المحدث ببرومات البوتاسيوم في الفئران. تلقت الفئران برومات البوتاسيوم بجرعة 20 ملجم/كجم من وزن الجسم، عن طريق الفم مرتين أسبوعيًا لمدة 4 أسابيع بمفردها أو مع المستخلصات المختلفة المختبرة يوميًا بجرعة 40 ملجم/كجم من وزن الجسم. أظهرت المستخلصات التي تم اختبارها أدوارًا وقائية للكلى تتميز بخفض مستوى الكرياتينين واليوريا وحمض البوليك وبروتين البول بالإضافة إلى زيادة البروتين الكلي في المصل والألبومين ومعدل تنقية الكرياتينين وحمض البوليك. وسجلت التأثيرات المعنوية لمستخلصات التمر هندي والخليط المختلفة خاصة الكحولية منها، في حين أن مستخلصات الكركديه قد تحتاج إلى جرعة و/أو فترة أعلى من تلك المستخدمة في هذه الدراسة. أظهرت النتائج أن التأثيرات الوقائية للمستخلصات ضد تسمم الكلى يعزى إلى أنشطة المركبات الفينولية مثل التأثيرات المضادة للأكسدة، والمضادة لارتفاع دهون الدم، والمضادة لتصلب الشرايين بالإضافة إلى تثبيط أكسدة الدهون والحمض النووي DNA بنسيج الكلي كما ظهر من نتائج المالونديالدهيد و8-هيدروكسي ديوكسي جوانوزين (8-OH-dG). أظهرت المستخلصات أيضًا تأثيرًا وقائيًا للكبد. ولذلك فمن الضروري تعزيز استخدام هذه النباتات، سواء كانت طازجة أو مجففة، إما كمشروبات أو لتدعيم الأغذية كملونات ومنكهات أو كتركيبات علاجية أو حتى في الطبخ عامة كما يستخدم عادة في العديد من البلدان. هناك حاجة إلى مزيد من الابحاث لاكتشاف الجرعة الآمنة المثالية ومدة الاستخدام.

الكلمات المفتاحية: *تمر هندي، كركديه، وظائف الكلي، صورة الدهون.*