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# Biochemical studies on some plant extracts as antitoxin on rats

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The chemical characterization and studying the antitoxin effects of *Rosmarinus officinalis* and *Matricaria chamomilla* extracts were as follows: Phytochemical screening, Total Polyphenols and Flavonoids content and Antitoxin effects on rats. Bio extracts were shown through color analysis containing phytochemical compounds such as (Terpens, Tannins, Flavonoids, Saponins, Alkaloids, Glycosides, Ph. Glycosides and Resins). Ethanolic extract of *R. officinalis* had the highest of total polyphenols and flavonoids contents, which were 152.00 mgGAE/g and 17.44 mgQE/g, respectively. It was followed by the aqueous extract of the same plant leaves, which were 139.08 mgGAE/g and 15.00 mgQE/g. The total polyphenols and flavonoids contents of ethanolic extract for *M. chamomilla*, were 144.00 mgGAE/g and 15.06mgQE/g. Next came the aqueous extract of the same plant leaves, which were, 127.11 mgGAE/g and 13.79 mgQE/g. The study showed the active effect of plant extracts as antitoxin when tested on rats. The results showed that the plant leave extracts increased the body weight, and improved antioxidant biomarkers and blood biochemical of rat.

**KEYWORDS**

*R. officinalis; M. chamomilla*; phytochemical; antitoxin and rat.

## Introduction

*Rosmarinus officinalis* L belongs to the family Lamiaceae, commonly known as rosemary [1]. Rosemary contains alkaloids, flavenoids, terpenoids, and essential oils [2-4]. The chemical analysis of extracts of different types of rosemary showed that the most potent components were phenolic acids, phenolic diterpenes, and triterpenes [3,5-7].

Rosemary has therapeutic characteristics and it has been used as an oral preparation to relieve dysmenorrheal, muscle spasm, and renal colic [5,8,9]. Rosemary has pharmacologic properties such as antibacterial, antiviral, antifungal, antitumor, anti-nociceptive, anti-inflammatory, antioxidant, antiulcerogenic, and antidepressant properties [8-10]. Rosemary is used for the treatment of the diseases associated with cardiovascular, nervous, genitourinary, menstrual, reproductive, hepatic, and gastrointestinal system [8].

*Matricaria chamomilla* L is commonly known as chamomile; it belongs to the family *Asteraceae*, and it has been used in traditional medicine [11]. Chamomile has been used in ancient Egypt, Rome, and Greece as herbal remedies [12]. The extraction of *Matricaria chamomilla* contains several bioactive antioxidant constituents [13]. *Matricaria chamomilla* has several pharmacological properties such as anticancer, anti-inflammatory, and immunomodulatory, antioxidants, chemo-preventive, and anti-platelets properties [13,14].

Doxorubicin (DOXO) belongs to the anthracycline group. It is an antitumor

antibiotic. DOXO has high efficacy as anti-neoplastic drug for the treatment of several cancers among adults and pediatrics such as breast cancer, solid tumors, soft tissue tumors, lymphoma, and leukemia [15]. DOXO is associated with severe cytotoxic adverse effects [16,17]. The chemotherapeutic agents cause cardio cytotoxicity which occurs in more than 20% of DOXO treated patients. The risk of developing cardiomyopathy is dose-dependent [18,19]. Peroxidation of endogenous lipids was shown to be the major contributor in the cytotoxic process of DOXO [20]. This study was conducted to study the impact of *Rosmarinus officinalis* and *Matricaria chamomilla* extracts on DOXO-induced cardio cytotoxicity.

## Materials and methods

*Plant materials*

Samples of *R. officinalis, M. chamomilla* were obtained from Agricultural Research Center, Giza, Egypt. Samples were dried in an oven at 55°C and ground into a fine powder. The powder was used for ethanolic and aqueous extract.

The aqueous extracts: 250 gm of dried samples were extracted with distilled water by boiling at temperature from 80 to 100 °C in reflux for 3 h to achieve an initial extract. The extracts were filtered after cooling to room temperature. Finally, the extracts were lyophilized and preserved at −20 °C until further use [21].

The ethanolic extracts: 1 Kg powder of each plant was extracted by soaking at room temperature for six times with ethanol (10 L), then the successive extraction was carried out by using ethanol. Extracts were obtained and then concentrated to dryness under vacuum and reduced pressure using the rotary evaporator at 45 °C to achieve the dried ethanol extracts which were kept at 4 °C till further use [22].

The yield of samples was 21.44, 20.01, 19.00 and 17.00%, of ethanolic and aqueous extracts, respectively.

Scientific classification

Kingdom: Plantae
Subkingdom: Tracheobionta

| | | |
|---|---|---|
| Family: | Lamiaceae | Asteraceae |
| Genus: | *Rosmarinus* L. | Matricaria L. |
| Species: | *Rosmarinus officinalis* L. | *Matricaria chamomilla* L. |

*Preliminary phytochemical tests of leave extracts*

Preliminary phytochemical tests were carried out on the extracts to detect the presence of terpenes, tannins, flavonoids, saponins, alkaloids, carbohydrates and/or glycosides, phenolic glycosides and resins.

**Detection of terpenes** [23]. A small amount of plant extract was dissolved in chloroform, then few drops of concentrated sulfuric acid were added carefully on the wall of test tube to form two separated layers, the resulted yellow ring changed to orange then red indicating the presence of terpenes.

**Detection of tannins** [23]. Few milliliters of distilled water were added to few milliliters of extract and filtrate, then, ferric chloride solution (5%) was added to the filtrate. The presence of tannins was indicated by the appearance of yellowish green color was obtained.

**Detection of flavonoids** [23]. A small amount of plant extract was macerated in

hydrochloric acid (1%) overnight, then sodium hydroxide solution (10%) was added to the filtrate. The appearance of yellow color indicated the presence of flavonoids.

**Detection of saponins** [23]. The plant extract was vigorously shaken developing a voluminous froth which persisted for almost one hour indicated the presence of saponins.

**Detection of carbohydrate and/or glycosides** [23]. Some drops of α-naphthol in ethyl alcohol were added to 1mL of extract, then 1 mL of concentrated sulfuric acid was added carefully without shaking. A purple ring appeared indicating the presence of carbohydrates and/or glycosides in crude plant extract.

**Detection of alkaloids** [23]. 2 mL of diluted hydrochloric acid was added to 1 mL of plant extract. Then five drops of Wagner's reagent were added to 1 mL of the solution and shaking after addition of each drop. After leaving for sometimes, it precipitated indicating the presence of alkaloids.

**Detection of phenolic glycosides** [23]. Some drops of concentrated sulfuric acid were added to 1mL of plant extract. A red color was produced then disappeared when water was added.

**Detection of resins** [23]. The extract was boiled on water bath for 20 minutes and distilled water was added to extract. In the presence of resins, a white precipitate was formed.

*Total phenolic contents*

Total phenolic contents of plant leave extracts were determined by using Folin–Ciocalteu reagent method according to Lin and Tang [24]. Aliquots of 0.1 mL from the solution was taken and mixed with 2.8 mL of distilled water, 2.0 mL of (2% w/v) sodium carbonate and finally 0.1 mL of 50% (v/v) of Folin–Ciocalteu reagent was added. The mixture was incubated for 30 minutes at room temperature and the absorbance of the resulting color was measured at 750 nm against distilled water as blank, using a Spekol 11 (Carl Zeiss-Jena) spectrophotometer. For quantitative determination, a standard curve of Gallic acid (0-200 mg/l) was prepared in the same manner. Total phenolic contents were expressed as milligram gallic acid equivalent (GAE)/g based on dry weight.

*Total flavonoid contents*

Total flavonoid contents of plant leave extracts were determined calorimetrically using aluminum chloride as described by Chang *et al.,* [25]. Resulting solution (0.5 mL) was mixed with 1.5 mL of 95% ethyl alcohol, 0.1 mL of 10% aluminum chloride ($AlCl_3$), 0.1 mL of 1M potassium acetate ($CH_3COOK$) and 2.8 mL of distilled water. After incubation at room temperature for 40 min, the reaction mixture absorbance was measured at 415 nm against distilled water as blank, using a Spekol 11 (Carl Zeiss-Jena) spectrophotometer. Quercetin was chosen as a standard of flavonoids for making the standard curve (0–50 mg/l). The concentrations of total flavonoids contents were expressed as milligram quercetin equivalent (QE)/g based on dry weight.

**Antitoxin activity**

*Experimental animals*

A number of 60 rats (175-200 g) were obtained from the animal house of [SAER], Egypt. The rats were kept for adaptation under normal laboratory conditions for 7 days before the beginning of the experiment. All rats were fed on balanced basal diet and allowed free access of water.

*Experimental design Komolafe et al., (26) and El-Sayed et al., (27):*

In the experimental design the rats were assigned into eight groups of six animals each:
Group 1: Normal group (SA, n=6) was given saline (1 mL/kg body weight).
Group 2: Control group (SA, n=6) was given saline (1 mL/kg)+DOX (15 mg/kg bw).
Group 3: Aqueous extract of *R. officinalis* (100 mg/kg bw).
Group 4: Ethanolic extract of *R. officinalis* (100 mg/kg bw).
Group 5: Aqueous extract of *M. chamomilla* (100 mg/kg bw).
Group 6: Ethanolic extract of *M. chamomilla* (100 mg/kg bw).
Group 7: Aqueous extract of *R. officinalis* (100 mg/kg bw)+DOX (15 mg/kg bw).
Group 8: Ethanolic extract of *R. officinalis* (100mg/kg bw)+DOX (15 mg/kg bw).

Group 9: Aqueous extract of *M. chamomilla* (100 mg/kg bw)+DOX (15 mg/kg bw).
Group 10: Ethanolic extract of *M. chamomilla* (100 mg/kg bw)+DOX (15 mg/kg bw).

Plant leaves extracts (100 mg/kg bw aqueous and ethanolic) was administered orally to healthy experimental rats once daily for 9 consecutive days and thereafter, the rats were challenged with single intraperitoneal dose of doxorubicin (15 mg/kg bw) on the 7th day according to El-Sayed *et al.* [27]. Animals were sacrificed 48 h after doxorubicin administration to harvest serum and heart tissues which were used for various biochemical analyses.

Blood samples were collected from the tail canthus by heparinized tubes. Then, each blood sample was centrifuged (10000 rpm) to obtain clear serum where serum glucose levels for fasting animals were determined immediately. Serum blood samples were kept at refrigerator under freezing conditions for the determination of the other parameters.

*Determination of plasma biochemical parameters*

Lactate dehydrogenase (LDH) was determined according to Lum and Gambino [28]. Creatine phosphokinase (CK) was estimated according to Tsung *et al.* [29]. Aspartate aminotransferase (AST) was evaluated according to Reitman and Frankel [30].

*Determination of antioxidant activity*

Malondialdehyde (MDA) was investigated according to Ohkawa *et al.* [31]. Superoxide Dismutase (SOD), was estimated according to Kakkar *et al.* [32]. Reduced glutathione (GSH) was assessed according to Sedlak and Lindsay [33]. Glutathione S-transferase (GST) was estimated according to Haque *et al.* [34]. Glutathione Peroxidase (GPx) and Glutathione reductase (GR) were determined according to Mohadas *et al.* [35].

*Statistical analysis*

Statistical analyses of all experimental data were done using the statistical software package CoStat [36]. All comparisons were first subjected to one-way analysis of variance (ANOVA) and significant differences between treatment means were determined using Duncan's multiple range test at $P<0.05$ as the level of the significance Duncan [37].

## Results

In this study the preliminary tests of the two plants under investigation showed presence of terpenes, tannins, flavenoids, saponins, alkaloids, glycosides, ph.glycosides and resins. The concentrations of alkaloids, glycosides, ph.glycosides and resins were similar in the two plants regarding the aqueous and ethanolic extractions. The details of the preliminary tests are shown in Table1.

**TABLE 1** Preliminary phytochemical tests (Qualitative)of plant extracts

| Plant leaves extracts | | Terpens | Tannins | Flavonoids | Saponins | Alkaloids | Glycosides | Ph. glycosides | Resins |
|---|---|---|---|---|---|---|---|---|---|
| *R. officinalis* | *Aque* | + | + | ++ | ++ | ++ | ++ | ++ | + |
| | *Eth* | ++ | ++ | +++ | +++ | ++ | ++ | ++ | + |
| *M. chamomilla* | *Aque* | ++ | + | ++ | ++ | ++ | ++ | ++ | + |
| | *Eth* | ++ | ++ | ++ | ++ | ++ | ++ | ++ | + |

(-)= negative results, (+) = positive results, (+++) = Strongly positive results. Conditions are classified depending on the concentration of the active ingredient in the solution by Spectrophotometer

*Total polyphenols and total flavonoids content of plant extracts*

The investigation of the total polyphenols and total flavonoids showed that the concentration of the total polyphenols was higher in the ethanolic extraction (152,144 mg/GAE/g for *R. officinalis*, and *M. chamomilla*, respectively) compared with the aqueous extraction in both plants (139.08, 127.11 mg/GAE/g for *R. officinalis*, and *M. chamomilla*, respectively). Also, the concentration of total flavonoids was higher in the ethanolic extraction (17.44,15.06 mg/QE/g for *R. officinalis*, and *M. chamomilla*, respectively) compared with the aqueous extraction (15,13.79 mg/QE/g for *R. officinalis*, and *M. chamomilla*, respectively) (Table2).

**TABLE 2** Total polyphenols and total flavonoids content

| Plant leaves extracts | | Total Polyphenols (mg GAE/g) | Total Flavonoids (mg QE/g) |
|---|---|---|---|
| *R. officinalis* | *Aque* | 139.08 | 15.00 |
| | *Eth* | 152.00 | 17.44 |
| *M. chamomilla* | *Aque* | 127.11 | 13.79 |
| | *Eth* | 144.00 | 15.06 |

*Effect of plant extracts on DOX induced changes in Body and heart weight*

The mean ±SD of the initial weight of the normal group was 190±0.02 g, which increased when evaluated at the end of the study to 225.4±0.01 g. The mean±SD of heart weight of the normal group was 0.630±0.002 g. The mean±SD of the initial weight and final weight of DOX group and *M. chamomilla* aqueous extraction with DOX group were the lowest compared with the other groups; 188.3±0.4 g, and 223.2±0.02 g for initial and final weight, respectively in the DOX group, 188±0.02 g, and 222±0.02 g for initial and final weight, respectively for the *M. chamomilla* aqueous extraction with DOX group. The mean±SD of the heart weight of the DOX group was 0.600±0.004 g and it was the least weight of heart reported among all the studied groups. Also, DOX group showed the least ratio of heart weight/body weight; 0.280±0.002 g, Table 3.

**TABLE 3** Effect of plant extracts on DOX induced changes in heart weight and heart weight to body weight percentage

| Groups | Initial Body weight (g) | Final Body weight (g) | Heart weight (g) | Heart weight/ body weight (g) |
|---|---|---|---|---|
| Normal | 190.0 ±.02 | 225.4±.01 | 0.630±.002 | 0.335±.004 |
| Doxorubicin (DOX) | 188.3 ± 04 | 223.2±.02 | 0.600±.004 | 0.280±.002 |
| *R. officinalis* (AE) | 192.0±.00 | 225.0±.02 | 0.626 ±.006 | 0.330±.006 |
| R. officinalis (EE) | 192.0±.02 | 225.1±.04 | 0.628 ±.004 | 0.332±.004 |
| *M. chamomilla*(AE) | 191.0±.00 | 224.1±.00 | 0.625±.002 | 0.328±.002 |
| *M. chamomilla*(EE) | 191.0±.04 | 224.2±.00 | 0.626±.002 | 0.330±.004 |
| *R. officinalis* (AE) +DOX | 189.0±.02 | 222.4±.06 | 0.618±.002 | 0.320±.002 |
| *R. officinalis* (EE) + DOX | 190.2±.00 | 224.0±.02 | 0.620±.004 | 0.322±.006 |
| *M. chamomilla* (AE) + DOX | 188.0±.02 | 222.0±.02 | 0.616±.002 | 0.319±.004 |
| *M. chamomilla* (EE) + DOX | 189.0±.04 | 223.0±.04 | 0.618±.006 | 0.321±.002 |

*Effect of plant extracts on DOX-induced changes in various antioxidant biomarkers*

The effect of the plant extracts and DOX on several antioxidant biomarkers are shown in Table 4. The mean± SD of GSH, GST, GPx, GR, and SOD in the DOX group was12.88, 108.12, 78.24±0.05, and 5±0.02, respectively. These values were the lowest compared with the values of the same biomarkers in the other

groups. The mean ±SD of MDA increased compared with the other groups 22.02 reflecting the highest oxidative stress.

**TABLE 4** Effect of plant extracts on DOX-induced changes in various antioxidant biomarkers

| Groups | (GSH) (µ mole/g tissue) | (GST) (n M /mg tissue) | (GPx) (n M /mg tissue) | (GR) (n M /mg tissue) | (MDA) (U/mg tissue) | (SOD) (U/mg tissue) |
|---|---|---|---|---|---|---|
| Normal | 20.68±00 | 140.86±00 | 118.44±00 | 150.02±04 | 18.44±02 | 9.41±04 |
| Doxorubicin (DOX) | 12.88±00 | 108.12±00 | 78.24±05 | 102.33±00 | 22.02±00 | 5.00±02 |
| *R. officinalis* (AE) | 20.22±04 | 141.02±02 | 119.00±00 | 152.01±00 | 18.05±00 | 9.08±00 |
| R. officinalis (EE) | 20.54±02 | 142.17±00 | 120.14±02 | 154.00±00 | 18.23±04 | 9.12±01 |
| *M. chamomilla*(AE) | 20.06±04 | 140.12±00 | 118.02±00 | 150.44±00 | 17.88±00 | 9.06±00 |
| *M. chamomilla*(EE) | 20.25±01 | 136.04±00 | 119.66±00 | 152.00±02 | 18.07±00 | 9.10±01 |
| *R. officinalis* (AE)+DOX | 18.04±02 | 132.00±00 | 112.00±00 | 141.00±00 | 20.01±00 | 7.96±02 |
| *R. officinalis* (EE)+DOX | 19.00±00 | 135.03±01 | 114.01±00 | 143.00±01 | 19.03±02 | 8.22±00 |
| *M. chamomilla* (AE)+DOX | 17.94±00 | 131.00±00 | 109.04±00 | 139.01±02 | 20.15±00 | 7.44±04 |
| *M. chamomilla* (EE)+DOX | 18.49±02 | 133.02±01 | 112.06±02 | 142.04±00 | 19.54±01 | 8.12±00 |

*Effect of plant extracts on toxic substances (DOX-induced) of blood biochemical in rats*

The impact of plant extracts on the biochemical markers are shown in Table 5. The mean ±SD of LDH was 390.22±0.04 in the normal group. This value increased significantly in the DOX group 530.44±0.6, whereas it reduced significantly in the *M. chamomilla* aqueous extraction 382.77±0.04. The mean± SD of CK in the normal group was 352.06, and it increased significantly in the DOX group 620.16, whereas it significantly reduced in the two groups of the aqueous extraction of *R. officinalis* 349.2±0.07, and *M. chamomilla* 349. The same was found regarding the AST mean level. The mean ±SD of AST in the normal group was 132.12±0.02, and it increased significantly in the DOX group to 212.02, whereas it reduced in the groups of aqueous extraction of *R. officinalis* 131.12±0.02, and *M. chamomilla* 349131±0.01.

**TABLE 5** Effect of plant extracts on toxic substances (DOX-induced) of blood biochemical in rats

| Groups: | (LDH) (IU/L) | (CK) (IU/L) | (AST) (U/L) |
|---|---|---|---|
| Normal | 390.22±04 | 352.06±00 | 132.12±02 |
| Doxorubicin (DOX) | 530.44±06 | 620.16±00 | 212.02±00 |
| *R. officinalis* (AE) | 388.40±00 | 349.20±07 | 131.12±02 |
| R. officinalis (EE) | 391.00±02 | 353.00±00 | 133.00±00 |
| *M. chamomilla*(AE) | 382.77±04 | 349.00±00 | 131.00±01 |
| *M. chamomilla*(EE) | 389.44±06 | 352.02±00 | 132.18±00 |
| *R. officinalis* (AE)+DOX | 420.07±00 | 402.00±02 | 158.11±02 |
| *R. officinalis* (EE)+DOX | 400.03±00 | 372.29±00 | 140.14±04 |
| *M. chamomilla* (AE)+DOX | 429.33±02 | 405.01±00 | 162.33±02 |
| *M. chamomilla* (EE)+DOX | 415.01±00 | 381.07±001 | 144.39±05 |

## Discussion

In the current study, we investigated the two plants of rosemary and chamomile. The ethanolic and aqueous extractions of the two plants were found to contain similar concentrations of resins, ph.glycosides, glycosides, and alkaloids, whereas they

contained varied concentrations of terpenes, tannins, flavonoids, and saponins. The ethanolic extraction of rosemary contained higher concentrations of the previous compounds, whereas chamomile contained equal concentrations of such compounds in the ethanolic and aqueous extraction, except for tannins which was higher in the ethanolic extraction. Moreover, the concentrations of total phenols and total flavonoids were higher in the ethanolic extraction compared with the aqueous extraction of the two plants. It was reported that the extract of chamomile had high levels of polyphenols and flavonoids [38]. This study showed that the addition of ethanolic and aqueous extraction of the two plants did not increase the body weight of the animals, whereas the injection of DOX resulted in significant reduction in the body weight of animals. However, the ethanolic extract of the two plants inhibited the effect of DOX and assisted to retrieve the body weight to normal and near normal, where the ethanolic extraction of rosemary was more potent compared with the ethanolic extraction of chamomile. The extractions of the two plants did not cause increase in the heart weight, whereas DOX resulted in significant reduction the heart weight. However, the extractions of the plants resulted in inhibition of the DOX effect, with the ethanolic extractions being the most potent compared with the aqueous extractions. Also, the ethanolic extraction of rosemary was more potent compared with that of chamomile. The ratio of heart weight to body weight in turn was affected in the same manner.

Oxidative stress exerts its harmful effects through the production of free radicals, which destroy the cell membrane of the cells [39]. Antioxidants exert their effect through scavenging of such free radicals [39]. Oxidative stress also leads to inflammation which in turn results in chronic deregulation [40]. Antioxidant deficit and increased oxidative stress have been demonstrated to have a major role in Dox-induced cardiomyopathy and heart failure when DOX was used for multiple treatments [41].

The antioxidants investigated in this study included GSH, GST, GR, and SOD. We also investigated the MDA as a marker of the presence of oxidative stress. The DOX induced the damage by increasing the oxidative stress as MDA was found to be significantly increased in the DOX group compared with normal, whereas GSH, GST, GR, and SOD reduced significantly; this reflects the cytotoxic effect of the DOX. On the other side, the extracts of the two plants were kept under the normal state of these markers and had no cytotoxicity. Moreover, the plant extractions resulted in the restoration of the normal state of the cells in the animals injected by DOX. The ethanolic extractions of the two plants were more potent compared with the aqueous extractions. Also, the ethanolic extraction of rosemary was more portent compared with that of chamomile. This reflects the protective impact of rosemary and chamomile against the oxidative stress, showing their anti-inflammatory properties.

In agreement with our study, previous studies [38,42-44] reported that DOX reduced the cardiac content of GSH, SOD, and increased the cardiac MDA. It was reported that the ethanolic extraction of the chamomile flower improved the cardio cytotoxicity induced by DOX [38].

Another study reported that administration of DOX of a dose of 15 mg/Kg resulted in cardiomyopathy that was detected by the significant elevation of LDH and CK levels [45]. The administration of the aqueous extraction of rosemary leaves of 15 mg/Kg prior to DOX induction by two weeks showed no significant protection, and did not affect the levels of HDL and CK, whereas when the dose increased to 30 mg/Kg, a protective effect was found.

Regarding biochemical investigation, we investigated the levels of LDH, CK, and AST. Higher value of LDH indicates the presence of tissue damage, and it is more associated with the heart. The elevation if the CK indicates injury or stress in the heart [46]. In the DOX group, there was high elevation in the levels of LDH and CK reflecting heart damage. This impact of DOX was reduced by addition of the

two plant extracts. The ethanolic extracts of the two plants resulted in significant reduction compared with the aqueous extracts, whereas the ethanolic extract of rosemary was more potent compared with the ethanolic extract of chamomile, as the ethanolic extract of rosemary resulted in significant reduction in the enzymes compared with the ethanolic extract of chamomile.

Previous studies reported elevation in the activity of the cardiac enzymes in rats after a single cumulative dose of 15-20 mg/Kg of DOX [47-49]. A study from Saudi Arabia showed that DOX produced severe cardio cytotoxic effect could be determined by the significant increase in the cardiac enzyme LDH and CK [38]. Moreover, a study revealed that administration of the ethanolic extract of chamomile flowers could restore the enzyme activities near normal [38]. The previous findings were in line with our findings which were conducted on the leaves reflecting that the flowers and leaves of chamomile were effective against the cardiotoxicity caused by DOX.

In a study on the effect of aqueous extract of rosemary on DOX-induced cytotoxicity, it was found that administration of the aqueous extract of rosemary leaves before the DOX doses resulted in a reduction in the oxidative stress, and all doses of the rosemary aqueous extract significantly reduced the apoptotic index in the heart [50]. A study conducted using rosemary and cranberry extractions showed that the extraction of both plants inhibited the DOX-induced elevation in CK and the groups given cranberry or rosemary showed low levels of CK as control group [51].

## Conclusion

The ethanolic extracts of the two plants under study (Rosemary and chamomile) contained higher concentration of total phenols and total flavonoids compared with the aqueous extraction of the two plants. Also, the ethanolic extracts of the two plants inhibited significantly the cytotoxic effect of DOX, and assisted the body to restore its normal state. The ethanolic extracts had protective properties against the cardiotoxicity of the DOX, with the ethanolic extract of rosemary being the most potent extract. This can be explained by the fact that rosemary contains higher content of polyphenols and flavenoids compared with chamomile regarding both aqueous and ethanolic extractions.

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