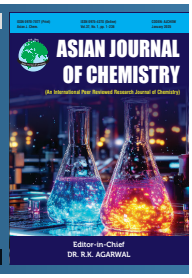
Asian Journal of Chemistry; Vol. 37, No. 7 (2025), 1673-1678

ASIAN JOURNAL OF CHEMISTRY

https://doi.org/10.14233/ajchem.2025.33867



Bioactive Potential of Toba Frankincense (*Styrax paralleoncomud* PERK) Fruit and Seeds Extracts: Phytochemical Profiling, Toxicity and Antioxidant Activity

M. SITORUS*, P. FARADILLA and R.D. SUYANTI

Department of Chemistry, State University of Medan, Medan, Indonesia

*Corresponding author: Tel: +62 82167726315; E-mail: marham@unimed.ac.id

Received: 12 April 2025; *Accepted*: 9 June 2025; *Published online*: 30 June 2025; AJC-22042

In this work, the phytochemical screening, toxicity test with BLST and antioxidant against free radicals DPPH of Toba frankincense fruit and seed extracts (STYRAX *parallel to PERX*) have been carried out. Secondary metabolites of the fruit are dominated by alkaloids, saponins, steroids and tannins, while in seeds, the alkaloids and terpenoids are dominated. Toxicity based on the LC_{50} value of fruit flesh extract *n*-hexane 117.91 ppm (toxic), ethyl acetate 43.15 ppm (toxic) and ethanol 16.95 ppm (highly toxic). For seeds extract *n*-hexane 42.22 ppm (toxic), ethyl acetate 20.12 (highly toxic) and ethanol 18.46 ppm (highly toxic). The antioxidant activity of the most toxic namely ethanol extract obtained LC_{50} values for fruit flesh was 150.35 ppm (moderate) and seeds was 434.04 ppm (weak). In general, the toxicity of fruit is higher than seeds and based on toxicity and antioxidants activity, fruit extracts have the potential as drugs, by further studying the antibacterial bioactivity properties.

Keywords: Frankincence, Phytochemical screening, Toxicity, Antioxidant activity.

INTRODUCTION

The Toba Frankincense plant (Styrax *paralleoncomud PERK*) is an endemic plant that grows in the area around Toba Lake, North Sumatra Province of Indonesia including Samosir, Dairi, Humbang Hasundutan, Toba and North Tapanuli Regencies [1]. In general, the part of the frankincense plant that is widely used for various industries, perfumes and medicines is its sap (resin). Frankincense sap contains secondary metabolites of the phenolic group such as benzoic acid, cinnamic acid, benzoyl cinnamate, alkaloids, flavonoids, saponins and triterpenoids [2]. Based on the metabolic pathway, secondary metabolites are spread throughout the plant tissue, but certain groups accumulate in certain tissues, such as frankincense, which is dominant in its sap [3]. Thus, the secondary metabolites found in the sap will also be found in the leaves and seeds of the frankincense plant [4].

Fruits and seeds are the origin of plant genetic reproduction, so it is believed that just like sap, bioactive secondary metabolites are also found in fruit flesh and seeds, which function as growth regulators [5]. Isolation was carried out by macerating the fruit flesh and frankincense seeds with *n*-hexane, ethyl acetate and ethanol solvents [6]. Furthermore, secondary metabolite analysis was carried out by phytochemical screening, namely by chemical tests using appropriate reagents [7]. Toxicity testing as a general test to determine bioactivity, especially its toxic properties, was carried out by using the brine shrimp lethality test (BSLT) method with *Artemia salina* Lech larvae as bioindicators [8]. Furthermore, the antioxidant activity test was carried out by testing the inhibition power against DPPH (2,2-diphenyl-1-1picrilhydrazyl) free radicals, which was measured by a visible spectrophotometer at a wavelength (χ) = 517 nm [9]. The toxicity criteria and antioxidant activity were determined based on the L_{50} value determined by the linear regression equation.

EXPERIMENTAL

Toba frankincense fruit flesh and seeds (Styrax *paralleoncomud PERK*) were procured from Sipahutar sub-district, North Tapanuli district of Indonesia. The chemicals used in this study were *n*-hexane, ethyl acetate, ethanol as a solvent, ferric chloride (5% and 1%, w/v), Dragendorff reagent, acetic anhydride, hydrochloric acid (2 N), conc. sulfuric acid, Whatman

40 mesh filter paper, Artemia *salina Leach* eggs, yeast and sodium chloride.

Isolation and phytochemical screening: Each fruit flesh and frankincense seeds were chopped and air-dried until free of water. Furthermore, two dried samples fruit flesh and seeds were ground into powder using a grinder blender and sieved with a 60 mesh sieve. A total of 200 g of each of the sieved fruit flesh and seed powders were successively macerated with *n*-hexane, ethyl acetate and ethanol solvents until there was no significant increase in colour intensity. For each solvent change, the residue was filtered with Whatman paper and all extracts were concentrated with a rotary evaporator. The alkaloid test was carried out by mixing 0.5 g of extract with 1 mL of 2 N HCl, 9 mL of distilled water and 5 drops of Dragendorff reagent, brick red precipitate indicated the presence of alkaloids. The flavonoid test was carried out by adding two drops of 5% $FeCl_3$ solution (w/v) to the sample on the drop plate. The occurrence of a colour change to greenish or black-blue indicates the presence of flavonoids. The saponin test is done by mixing 1 mL of sample with 10 mL of distilled water, shaking for 10 min until foam forms and then wating for 10 min. If the foam does not disappear, add 2 N HCl and if it can disappear, which indicates the presence of saponin compounds. Steroid and terpenoid tests are done by mixing 0.5 g of fruit pulp and seed powder with 10 drops of acetic anhydride, 2 drops of conc. H_2SO_4, shaking and left for a few minutes. The appearance of red and purple colours indicates the presence of terpenoids, if green and blue colours appear, it indicates the presence of steroids. The tannin test was done by mixing 0.5 g of extract with 10 mL of distilled water and 3 drops of 1% $FeCl_3$, the appearance of a blackish-green colour indicates the presence of tannins.

Toxicity properties: Larvae breeding was carried out by raising 1 g of *Artemia salina* Leach eggs. The eggs were hatched by soaking them in 2 L of artificial sea water and were illuminated with a 40-60 watt incandescent lamp and aerated for 48 h. Artificial sea water was made by dissolving 40 g of NaCl in 2 L of water and then filtered. Next, a stock solution of 2000 ppm fruit flesh and seeds was made. Next, a series of solutions were made with concentrations of 1000, 500, 100, 50 and 25 ppm from the stock solution. The control solution as a comparison used was without the addition of samples. Toxicity testing used 5 different concentration series, where 10 *Artemia salina* Lech larvae that were 48 h old were taken, put into a vial containing samples with the concentration series that had been made. Next, 3 mL of artificial sea water was added, then one drop of yeast suspension was added as food and artificial sea water was also added to a volume of 5 mL. Each test was accompanied by a negative control with three repetitions. The vial was kept to always get optimal lighting and after 24 h, the number of dead larvae. Toxicity was determined by the linear regression equation Probit value against to determine the amount of LC_{50} [10].

Antioxidant activity: A series of fruit flesh sample solutions (61.02; 122.04; 183.08; 61.02; 122.04; 183.08; 44.08 and 305.10 ppm) and a series of seed sample solutions (60.6; 121.2; 181.8; 242.4, 303.0; 363.6 and 484.8 ppm) with the control being a 0 ppm solution (without sample) were prepared. Each sample was added with 2 mL of DPPH radical solution with a quenching time of 30 min. Absorbance was measured using a visible spectrophotometer at an optimal wavelength of 517 nm with two repetitions and antioxidant activity was calculated using the following equation:

$$\text{Antioxidant activity (\%)} = \frac{A_{control} - A_{sample}}{A_{control}} \times 100$$

The value of IC_{50} (inhibition concentration) was determined based on the linear equation obtained through the Exel program inhibition graph (%) *versus* concentration (ppm).

RESULTS AND DISCUSSION

The results of the chopped water-free Frankincense fruit flesh are shown in Fig. 1a and the seeds are shown in Fig. 1b. Furthermore, powder with a particle size of 60 Mesh fruit flesh is shown in Fig. 1c and seeds are shown in Fig. 1d. The purpose of refining the particles to 60 mesh is so that the surface area of the contact area with the solvent is wider so that the results of the maceration are obtained will be maximized [11].

Furthermore, maceration was carried out on the fruit flesh powder and seeds with the order of *n*-hexane solvent (non-polar), ethyl acetate (semipolar) and ethanol (popar), to dissolve secondary metabolites according to their polarity [12]. Each time the solvent was changed, the residue was filtered with Whatman paper and the residue was air-dried before changing the solvent to clean the secondary metabolites extracted with the previous solvent. Maceration was carried out in a dark place so that secon-

Fig. 1. Results of chopping water-free fruit flesh (a), seeds (b) and results of sieving powder with a size of 60 mesh for fruit flesh (c) and seeds (d)

dary metabolites that are susceptible to light are not damaged through oxidation or decomposition reactions. Maceration was stopped if there was no significant increase in colour intensity [13]. The difference in filtrate colour indicates that the extracted secondary metabolite groups are different according to the similarity of polarity of the solvent and the extracted secondary metabolites [14].

The concentrated filtrate was determined for its secondary metabolite group through phytochemical screening. The alkaloid test was carried out by mixing 0.5 g of extract with 1 mL of 2 N HCl, 9 mL of distilled water was given 5 drops of Dragendorff's reagent and brick red precipitate indicated the presence of alkaloids. Thr flavonoid test was carried out by adding 2 drops of 5% $FeCl_3$ solution (w/v) to 5 drops of sample on the drop plate. The occurrence of a colour change to greenish or black-blue indicates the presence of flavonoids. The saponin test was carried out by mixing 1 mL of sample with 10 mL of distilled water, shaking for 10 min and leaving foam then waiting for 10 min, if the foam does not disappear, added 2 N HCl if it disappears indicating the presence of saponin compounds. The steroid and terpenoid tests were carried out by mixing 0.5 g of extract with 10 drops of acetic anhydride, 2 drops of conc. H_2SO_4, shaking and leaving for a few minutes, the appearance of red and purple colours indicates the presence of terpenoids, if green and blue colours appear indicate the presence of steroids. The test for the presence of tannins was carried out by mixing 0.5 g of extract with 10 mL of distilled water and 3 drops of 1% $FeCl_3$ (w/v), the appearance of a blackish green colour indicates tannins [15]. This phytochemical screening is in principle a chemical test with a reagent for testing functional groups of organic compounds, which are physically characterized by the formation of deposits and coloured complexes or also producing gas bubbles to foam such as alkene test with the bromine reagent. The presence of alkenes is indicated by the loss or reduction in the intensity of the orange colour from bromine [16]. The results of phytochemical screening on the flesh of the fruit and frankincense seeds are shown in Table-1.

Based on Table-1, the secondary metabolites of *n*-hexane extract of Toba frankincense fruit contain relatively high amounts of steroids. The ethyl acetate extract contains flavonoids and steroids, both in moderate amounts. The ethanol extract contains alkaloids, flavonoids, saponins, terpenoids and tannins, where the most dominant are alkaloids, saponins and tannins. Meanwhile, the secondary metabolite group in the *n*-hexane solvent seeds contains moderate amounts of terpenoids. The ethyl acetate extract contains alkaloids, flavonoids, saponins and terpenoids in moderate amounts and the most dominant are alkaloids and terpenoids. The ethanol solvent contains flavonoids, saponins, terpenoids and tannins in small amounts. Flavonoids in plants are pigments or colouring agents both in fruit and especially in leaves [17]. Alkaloid groups in some plants accumulate in seeds such as coffee and frankincense seeds are also obtained at high levels, especially in ethyl acetate solvents in fruit in ethanol solvents in seeds. This indicates that the alkaloids in seeds are more polar (small molecules) than in fruit [18].

Toxicity properties: In this study, the toxicity test of frankincense fruit and seed extracts was carried out using the BSLT (brine shrimp lethality test) method. First, the hatching of *Artemia salina* Leach eggs was carried out in an aquarium filled with 2 L of artificial seawater and 1 g of *Artemia salina* Leach eggs and left for 48 h for hatching. The aquarium was equipped with a 5 watt incandescent lamp to keep the seawater warm, thus accelerating the hatching process. Aeration was carried out using an aerator to provide sufficient oxygen for the survival of the larvae, so that hatching was faster. The *Artemia salina* Lech larvae used were newly hatched larvae, reddish in colour and still had food reserves, 24 h after hatching. Feeding was stopped when the larvae entered the first instar. Toxicity testing was carried out by diluting the extracts of *n*-hexane, ethyl acetate and ethanol stock 2000 ppm with concentration variations of 1000, 500, 100, 50 and 25 ppm with three repetitions. This concentration was used to determine the effect of differences in *Artemia salina* leach mortality at each concentration with the number of larvae inserted at 10 and observed after 24 h. The results obtained for the fruit extract are in Table-2 and the linear regression graph for calculating LC_{50} is in Fig. 2.

The probit value data is plotted with the concentration log in Table-2 to obtain a linear regression equation to calculate the LC_{50} value [19]. In general, the results obtained are that the increase in concentration is proportional to the increase in the number of deaths of *Artemia salina* Lech larvae. The LC_{50} value of fruit flesh with *n*-hexane solvent is 117.91 ppm (toxic), ethyl acetate solvent 43.15 ppm (toxic) and ethanol solvent 16.95 ppm (very toxic). The extract with the most toxic ethanol solvent is by the results of phytochemical screening containing large amounts of alkaloids, which are generally toxic. Toxicity is a general indication of the toxic nature (bioactivity) of a secondary metabolite. To find out more about the specific activity, this study conducted an antioxidant activity test [20]. Furthermore, the toxicity test data for the frankincense seed extract (Table-3) and to obtain the LC_{50} value, a graph of the

TABLE-1
RESULTS OF PHYTOCHEMICAL SCREENING OF TOBA FRANKINCENSE FRUIT FLESH AND SEED EXTRACTS (STYRAX *parelleoncomud PERK*) WITH *n*-HEXANE, ETHYL ACETATE AND ETHANOL SOLVENTS

Compound	Flesh of fruit			Seed		
	n-Hexane	Ethyl acetate	Ethanol	*n*-Hexane	Ethyl acetate	Ethanol
Alkaloid	Not detected	Not detected	Large amount	Not detected	Large amount	Not detected
Flavanoid	Not detected	Moderate	Small	Not detected	Small	Moderate
Saponin	Not detected	Not detected	Large amount	Not detected	Small	Small
Steroid	Large amount	Moderate	Not detected	Not detected	Not detected	Not detected
Terpenoid	Not detected	Not detected	Small	Moderate	Large amount	Small
Tanin	Not detected	Not detected	Large amount	Not detected	Not detected	Small

TABLE-2
EFFECT OF VARIATIONS IN THE CONCENTRATION OF TOBA FRANKINCENSE FRUIT FLESH EXTRACT (SYRAX *paralleoncomud PERK*) ON THE DEATH OF SHRIMP LARVAE (*Artemia salina* Leach)

Solvent	Concentration (ppm)	Log concentration	Number of larvae	Number of dead larvae	Death rate (%)	Probit value	LC_{50}
n-Hexane	25	1.40	30	10	33	4.56	117.91
	50	1.70	30	13	43	4.82	
	100	2.00	30	16	53	5.08	
	500	2.70	30	17	57	5.18	
	1000	3.00	30	22	73	5.61	
Ethyl acetate	25	1.40	30	9	30	4.48	43.15
	50	1.70	30	17	57	5.18	
	100	2.00	30	22	74	5.64	
	500	2.70	30	30	100	7.37	
	1000	3.00	30	30	100	7.37	
Ethanol	25	1.40	30	20	33	4.56	16.95
	50	1.70	30	23	77	5.74	
	100	2.00	30	30	100	7.37	
	500	2.70	30	30	100	7.37	
	1000	3.00	30	30	100	7.37	

TABLE-3
EFFECT OF VARIATIONS IN THE CONCENTRATION OF TOBA FRANKINCENSE SEED EXTRACT (STYRAX *paralleoncomud PERK*) ON THE MORTALITY OF SHRIMP LARVAE (*Artemia Salina* Leach)

Solvent	Concentration (ppm)	Log concentration	Number of larvae	Number of dead larvae	Death rate (%)	Probit value	LC_{50}
n-Hexane	25	1.40	30	13	43	4.82	42.22
	50	1.70	30	16	53	5.08	
	100	2.00	30	18	60	5.25	
	500	2.70	30	20	67	5.44	
	1000	3.00	30	22	73	5.61	
Ethyl acetate	25	1.40	30	15	50	5	20.12
	50	1.70	30	21	70	5.52	
	100	2.00	30	25	90	6.28	
	500	2.70	30	29	97	6.88	
	1000	3.00	30	30	100	7.37	
Ethanol	25	1.40	30	16	53	5.08	18.46
	50	1.70	30	22	73	5.61	
	100	2.00	30	27	90	6.28	
	500	2.70	30	30	100	7.37	
	1000	3.00	30	30	100	7.37	

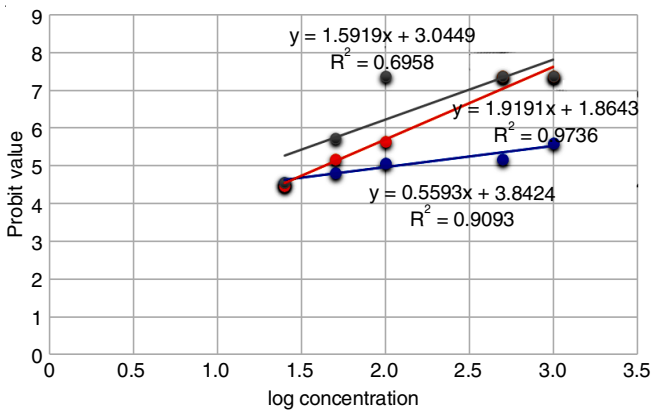


Fig. 2. Graph between probit value *versus* log concentration of Frankincense fruit flesh extract (STYRAX *paralleoncomud PERK*) with *n*-hexane, ethyl acetate and ethanol

probit value *versus* log concentration was made to obtain a linear regression equation as in Fig. 3.

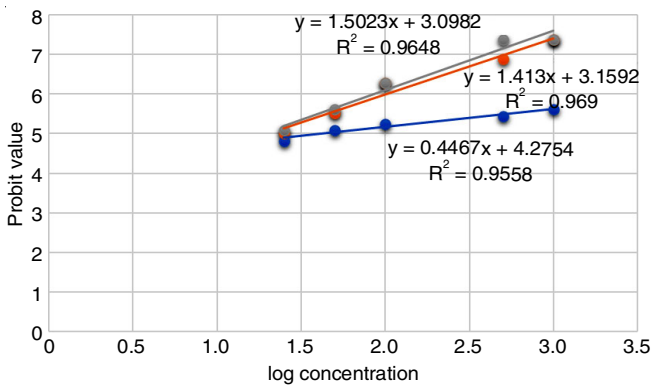


Fig. 3. Graph between probit value *versus* log concentration of Frankincense seed extract (STYRAX *paralleoncomud PERK*) with *n*-hexane, ethyl acetate and ethanol solvents

Based on Table-3 and linear regression in Fig. 3, the LC_{50} value for seeds with *n*-hexane solvent is 42.22 ppm (toxic), ethyl acetate solvent 20.12 ppm (highly toxic) and ethanol

TABLE-4
RESULTS OF TESTING THE ACTIVITY OF ETHANOL EXTRACT OF FRUIT FLESH (STYRAX *paralleoncomud PERK*) WITH DPPH FREE RADICALS

Concentration (ppm)	Absorbance			Inhibition (%)		
	Repeat 1	Repeat 2	Average	Repeat 1	Repeat 2	Average
0.0	0.91	0.91	0.91	0.00	0.00	0.00
61.02	0.68	0.64	0.65	25.38	30.09	27.24
122.04	0.47	0.47	0.47	48.03	49.18	48.60
183.06	0.31	0.36	0.33	65.96	61.10	65.53
244.08	0.20	0.19	0.19	77.89	79.41	78.65
305.10	0.12	0.15	0.13	86.22	84.02	80.19

TABLE-5
DATA ON ANTIOXIDANT ACTIVITY TESTING OF ETHANOL EXTRACT OF SEEDS (STYRAX *paralleoncomud PERK*) WITH DPPH FREE RADICALS

Concentration (ppm)	Absorbance			Inhibition (%)		
	Repeat 1	Repeat 2	Average	Repeat 1	Repeat 2	Average
0.0	0.91	0.91	0.91	0.00	0.00	0.00
60.60	0.87	0.87	0.87	4.50	4.07	4.28
121.20	0.77	0.78	0.77	15.65	15.18	15.42
181.80	0.69	0.70	0.69	24.41	23.94	24.18
242.40	0.62	0.63	0.63	32.05	31.12	31.58
303.00	0.57	0.55	0.55	37.02	39.79	38.41
363.60	0.55	0.54	0.54	40.39	40.49	40.44
484.80	0.43	0.43	0.43	52.69	52.69	52.75

solvent 18.46 ppm (highly toxic). The toxicity of seed extract generally exceeds that of fruit flesh, with the exception of the ethanol solvent; yet, both remain in the very toxic category, despite their differences being negligible [21].

Antioxidant activity: In this study, the antioxidant properties of the toxic frankincense fruit and seed extracts were tested, namely ethanol solvents with a highly toxic category with LC_{50} = 16.95 ppm for fruit flesh and 18.46 ppm for seeds. The antioxidant properties were tested with DPPH free radicals measured by visible spectrophotometer at 517 nm with 30 min attenuation time with two repetitions [22,23]. The results of fruit flesh and seed ethanol extracts are shown in Tables 4 and 5. The LC_{50} antioxidant activity of the ethanol extract of Frankincense fruit flesh (most toxic extract) was obtained at 150.35 ppm (moderate antioxidant category). In general, Frankincense fruit is not commonly consumed, so a study is needed on Frankincense fruit for consumption and also as a medicinal preparation since it has moderate antioxidant activity. Furthermore, the LC_{50} antioxidant activity of the ethanol extract of frankincense seeds is 434.04 ppm (not antioxidant). Seeds are parts of plants for generative reproduction that contain growth regulators, which are primary metabolites so they are not bioactive [24,25].

Conclusion

The secondary metabolite groups present in the fruit flesh and frankincense seeds are relatively the same, namely in the fruit flesh are flavonoids, saponins, steroid and tannins while in the seeds are alkaloids, flavonoids and terpenoids. The toxicity category of secondary metabolites with LC_{50} values for the fruit flesh of frankincense with *n*-hexane solvent is 117.91 ppm (toxic), ethyl acetate 43.15 ppm (toxic) and ethanol 16.95 ppm (very toxic). The LC_{50} value for seeds with *n*-hexane solvent is 42.22 ppm (toxic), ethyl acetate 20.12 ppm (very toxic) and ethanol 18.46 mg/L (very toxic). The antioxidant activity of secondary metabolites with ethanol solvent (the most toxic) is obtained by the LC_{50} value for the fruit flesh is 150.35 ppm (moderate antioxidant) and for seeds 434.04 ppm (not antioxidant). Based on the results of toxicity tests and antioxidant tests, the secondary metabolite extract of Frankincense fruit flesh has sufficient potential to be studied as a drug and to complete the bioactivity data, its antibacterial activity needs to be tested.

ACKNOWLEDGEMENTS

Thanks are expressed to UNIMED, who funded this research through the Medan State University DIPA Fund for Fiscal Year 2024 with Contract Letter No. 0047/UN33.8/PPKM/PD/20224. Thanks are also expressed to Unang Supratman Head of the Central Laboratory of Universitas Padjadjaran, Bandung, who helped test the antioxidant properties of the ethanol extract of Frankincence fruit flesh and seeds.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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