Egyptian Journal of Basic and Applied Sciences 5 (2018) 265–279

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Contents lists available at ScienceDirect

Egyptian Journal of Basic and Applied Sciences

journal homepage: www.elsevier.com/locate/ejbas

In silico prediction of anticarcinogenic bioactivities of traditional anti-inflammatory plants used by tribal healers in Sathyamangalam wildlife Sanctuary, India

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ARTICLE INFO

Article history:
Received 28 May 2018
Received in revised form 14 October 2018
Accepted 18 October 2018
Available online 26 October 2018

Keywords:
Ethnomedicine
Inflammation
Anticancer
In silico

ABSTRACT

The present study was designed to explore ethnopharmacological anti-inflammatory plants in the anti-cancer drug development. From the specialized local herbalists of the study area, who were treating tumors using anti-inflammatory plants by considering as a type of inflammation and explaining the potential of anti-inflammatory plants in prevalence of early stage's cancer. Interaction results obtained from the herbalists, and *in silico* PASS and CLC-pred prediction results were greatly agreed with documented data. Documentation was done through semi-structure standard designed proforma from the selected herbalist in study locality. A number of active compounds selected from recorded plants subsequently analyzed by using computational *in silico* tools such as PASS, admetSAR, and CLC-pred to investigate the antineoplastic capacity of anti-inflammatory plants. About 18 out of 20 plants said to be used in tumor-related affliction recognized for antineoplastic capacity using PASS database with high probability. Similarly, the selected compound's absorption, metabolism, and toxicity also predicted using the admetSAR tool. CLC-pred Tools performed to examine the different cell line cytotoxicity of compounds with respective probabilities.

1. Introduction

Ethnopharmacology becomes an important field to elucidate and justify the indigenous medicinal benefits bioactive of plant compounds through various biochemicals and experimental models [1]. India is one among the country which has potent knowledge of ancient treatment of medicinal plants. Tribal people encompass vast recognition of treatment by plant therapy, and their historical knowledge has guaranteed results over novel experimental studies of plants secondary metabolites as a source to draw anti-inflammatory drugs [1–3]. Wound inflammation, especially chronic wound is considered as a freighting issue on physical welfare, which is tough one to cure. Plant based medicaments are advised because of easy accessibility and better wound healing property of compounds [4,5]. India has documented 45,000 series of plants roughly 7500 species reputable as medicinal plants. Earlier system of Indian medicine "Ayurveda" describes healing properties as 'Vranaropaka' and treated with medicinal plants [6,7].

Cancer, a complicated disease holds the second position to cause death in all over the globe, and the incidences were discovered high in western countries comparatively than Asian countries. Ayurveda explains continuous irritation may lead to cancer under Granthi or Arbuda (inflammatory disease) that is a neoplasm will have the possibility to develop the malignancy and can treatable at early stage [8]. Due to the competence of preventing cancer, plants based compounds, which possess anti-inflammatory activity, are also used in cancer treatment [9]. Probably customary medicines are worked based on the synergistic effect of whole plant extract while modern medicines isolate a single plant compound [10,11].

Computational tools have become very much important in medicinal chemistry to predict the bioactivities of particular compounds based on structure–activity relationships, which are significantly correlated with experimental results [12]. The physical and chemical properties of plant based compounds were analyzed using *in silico* prediction models for their effective absorption metabolism and toxicity. These *in silico* techniques combined with pharmacology studies would greatly influence in discovery of novel drugs for ailments [13,14].

In the present study an attempt made to predict the anticarcinogenic activity of compounds presented in plants with wound

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https://doi.org/10.1016/j.ejbas.2018.10.002
2314-808X/

healing anti-inflammatory to explore the new plant compounds for anticancer activity through *in silico* studies. This also rationally proceeds towards interdisciplinary understanding of developing anticancer drugs from wound healing plants existed in traditional practices.

2. Materials and methods

2.1. Study area and tribal ethnography

Sathyamangalam wildlife sanctuary lies between Tamil Nadu and Karnataka boundary regions with 77° 15′ 0″ E longitude and 11° 31′ 11″ N latitude. Vegetation of the forest varies from tropical to temperate zones this forest extends east from Nilgiris. The thicket jungle is one of the piece elements of Western Ghats enhanced with diverse species of plant and animal covers about 1411.6 km^2 (545.0 sq mi) [15–17]. The moderate annual rainfall of the Sathyamangalam wildlife sanctuary is 824 mm, which located between the Western Ghats and the Eastern Ghats like a bridge. Wildlife Institute of India categorized the sanctuary as Eastern Ghats province in Biogeography classification (Fig. 1).

The forest is diversified with various tribal communities, including Irulas, Soligas, Kurumbas, Urali and also least distributed communities of Malayalee and Naickers. Urali is one of the dominants locale's tribal groups migrated and largely settled in Sathyamangalam forest with Urali language. The villager's main job is to sell the forest products such as honey, fuel wood, resins and medicinal herbs.

2.2. Data collection

The importance of each plant species among ethnic people was determined by use value (UV). The use value to a species (UV) is the summation over the number of use reports for the specific plant species (U) and is divided by the total number of informants (N) interviewed. If the use value is high, it indicates the many use reports and importance to the plant, and low value indicates the less use reports. This was calculated as follows.

$$UV = \sum UR/N$$

2.3. Identification of plant specimens

Identification of collected plant materials was performed by referring different regional floras and pertinent literature such as Flora of the Presidency of Madras, Flora of Tamil Nadu and Flora of the Tamilnadu Carnatic [18–20]. Then the plant materials were poisoned, pressed and preserved in a standard herbarium sheet. The collected specimens were compared and identified by the Madras herbarium (MH) Botanical Survey of India, Southern Regional Centre, Coimbatore, India. Further the confirmation made using The Plant List and International Plant Name Index [21,22] and Fig. 2 provides the identified plants.

2.4. In silico prediction using PASS and ADMET

Computer-aided structure-activity based prediction studies in drug design helps to treat diseases with novel biomarkers. Prediction of activity spectra for substances (PASS) database comprised 46,000 biologically well-known active drugs and screening are performed before the establishment of an *in vitro* experiment. PASS gives the significant bioactivities of chemical compounds as Pa (Probable activity) and Pi (Probable inactivity) values to mention the compounds, whether they are active are inactive. The Pa values higher than 0.7 indicated this compound would be active in experiment and Pi values indicate theirs inactivate possibilities. The admetSAR chemoinformatics based tool used to predict absorption, metabolism, excretion, and toxicity of the particular compound. Based on these criteria, the outcomes of an *in vitro* experiment will lower the risk of negative results [13,14].

2.5. In silico prediction of cell line cytotoxicity with CLC-Pred tool

CLC-Pred Tools performed to predict cytotoxicity of tumor cell lines, and it is based on structure-cell line cytotoxicity relationships designed by PASS special training sets with leave-one-out cross-validation procedure. The accuracy of *in silico* prediction results significantly 96% matches with the results of *in vivo* experimental. The efficiency of compounds against cancer could be found and optimized using this PASS based CLC-Pred database in the future to develop potential anti-cancer drugs. Predicted cytotoxicity gives results against various human cell lines represented with Pa values if Pa value is >0.5 the probability of action is considerably high and whereas Pi value indicates inactivity [23].

3. Result and discussion

3.1. Demography and ethnography of informants

Informant's selection was done randomly of all communities from different tribal settlement areas. Among gathered peoples a total number of 35 informants selected after the primary group discussion in all settlement groups by their knowledge about the traditional treatments on wounds, inflammation, and cancer. The age of selected 35 informants varies from 45 to 65 years, including male (14) females (21). From the 35 informants, 10 healers were identified as herbalists among them 3 of were female and the rest were male (7) (Table 1). Between 10 herbalists, 8 herbalists (2 female; 6 males with >55 years old) were agreed to the statement that they are treating tumors with anti-inflammatory plants (Table 1). A formal questionnaire was prepared and orally asked to refer the definition of wounds and tumor, how the wounds and tumor will be treated; preparation method adopted, the procedure of administration, duration of administration, the local name of the tumor and wounds and types of tumor they experienced.

The interrogation confesses chronic inflammation wounds may develop into the tumor but in the early stage, this can be curable. They are terming cancer as Katti in local language and also interestingly the herbalists were treating tumors of specific organ includes uterine fibroids caused through heredity and irregular menstrual cycle, Gastric tumor caused by chronic inflammation and ulceration (Table 2). The understanding and informative views about cancer among tribal dwellers are greatly agreed to the literature statement of causes of cancer, and also the chronic wounds were treated with herbalist prescription [5,24], among tribal inhabitants these complications were treated carefully in order to avoid forming tumor from chronic inflammation. Based on this, the entire primary ethno botanical investigation figured out locales having trivial knowledge about tumor treating plants, which are also used during the wound healing and inflammation activities.

3.2. Anti-inflammatory plants in cancer

The individual with most use-reports was considered as common medicine for a particular ailment treatment. Based on the use-reports collected from ethnic people use value (UV) was calculated to highlight the usage priority, importance, recommendation and sharing medicinal knowledge about the particular species among the informants. In this study *Abutilon indicum* (L.) Sweet,. (UV-0.60), *Lawsonia inermis* L., *Lycopersicon esculentum* Mill

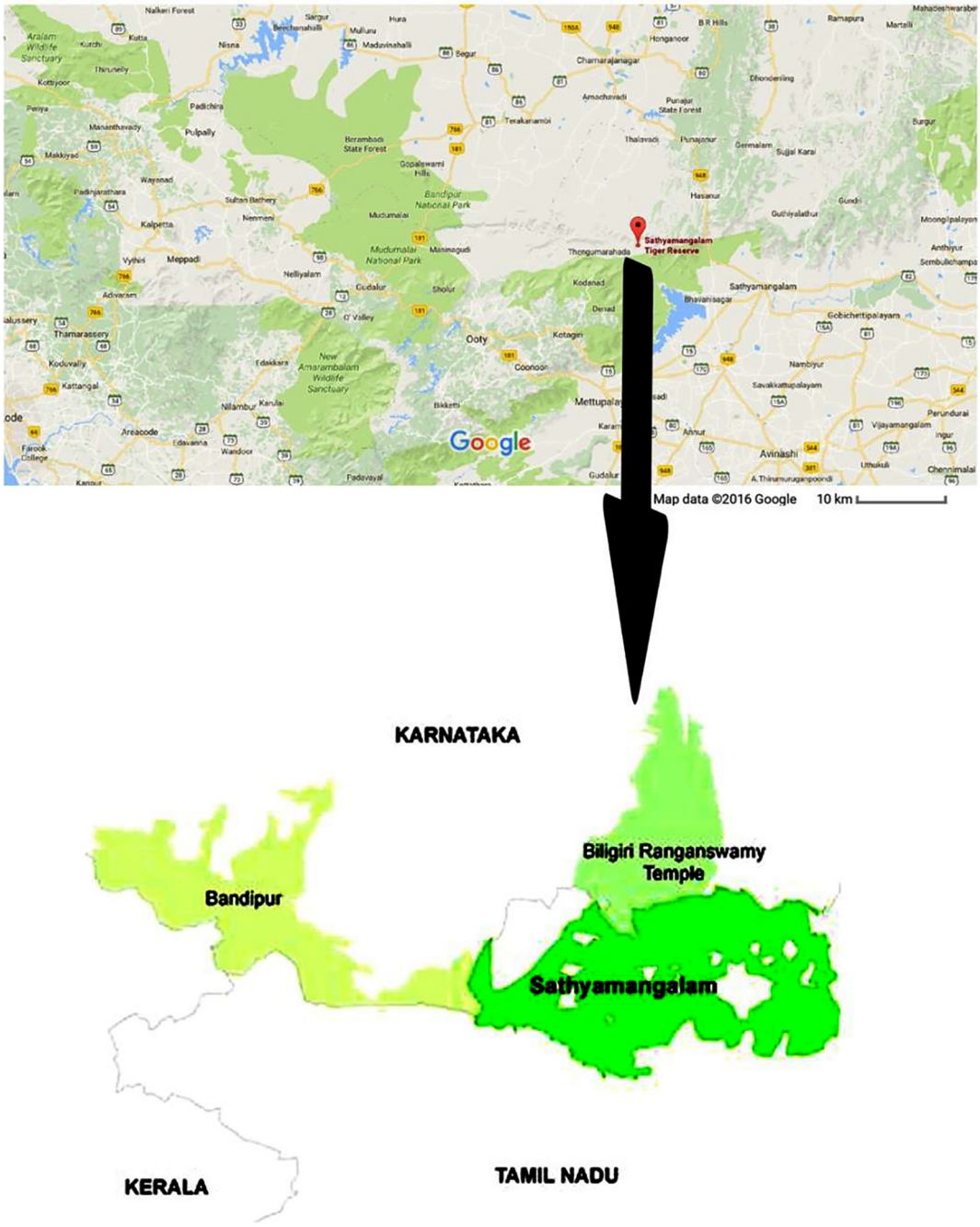


Fig. 1. Study area of the present study.

(UV-0.63), and *Madhuca indica* J.F.Gmel. (UV-0.66) showed commendable values this indicates the importance to the species among the studied area tribes (Table 3). However, least values indicate the limited knowledge of medicinal uses and may be due to its adverse effects of those plants.

Leaves are the dominant part used in the medicinal plant preparation for treating inflammatory, wounds and cancer from the study area followed by bark, seed, tuber, and whole plant part (Table 3). Basically, leaves are the uncomplicated plant part in collection and in systematic perspective leaves are loaded with the huge amount of metabolites comparing to other parts through the plant [25]. Present investigation comes out with the usage of adjuvant among the tribal community with 9 plants followed by 11 plants individual consumption (Table 3). The practice of utilizing adjuvants like honey, salt, milk and curd is a habit of Indian tribal inhabitants already reported for Taungya, Terai and Kani tribals in India. Usong adjuvants are technically for higher bioavailability, which leads for synergistic effect to cure the disease better [25,26]. The preparation methods for anti-inflammatory activity were mostly in dry powder form to treat wounds and skin tumors [7]. The other methods, including paste and decoction were used to treat skin and stomach ailments were treated with juice (Table 3) and extraction methods considerably uncommon to treat stomach and bladder problems [24].

3.3. *In silico* prediction results of PASS and admetSAR

In silico tools used for pre-screening of compound activities and direct the studies towards the prior designing of particular work. PASS is a well-known tool used in almost all pharmaceutical

Fig. 2. Some identified plants from the present study area.

Table 1
Demographic representation of interviewed tribes by age group in the study area.

Age group of informants (In years)	Local people		Herbalist	
	Male (14)	Female (21)	Male	Female
41–50	6	10		
51–60	7	5	6	2
61–70	1	6		

Table 2
List of biomedical terms used to identify the diseases with its corresponding local terms used by the tribes in the study area.

S. No	Biomedical terms	Local terms
1	Cancer	Katti
2	Uterus tumor	Karpa pai katti
3	Chronic inflammation	Vayitrupun katti
4	Inflammation	Udaleritchal
5	Burns	Theekkaayam
6	Wounds	Kaayam
8	Mouth ulcer	Vaaippun
9	Stomach ache	Vayitruvali
10	Stomach ulcer	Vayitrupun

industries which based on structure–activity relationship's analysis [27]. About 23 compounds corresponding to 20 plant species were selected and interpreted in PASS database to obtain the prediction of bioactivity. The collected 20 anti-inflammatory species which also observed to be used in tumor treatment by tribal inhabitants were predicted by PASS and indicated the existence of antineoplastic activity in 18 reported plants. The compound aristolochic acid from *Aristolochia bracteolate* Lam. showed higher probabilities for the antiseptic (0.968/0.002), respiratory analeptic (0.828/0.007) and apoptosis agonist (0.821/0.007) in prediction (Table 4) but various studies shows that aristolochic acid can be used on many types of cancer, including bladder cancer it closely resembles with the statement of usage of *Aristolochia bracteolate* Lam. in urinary track cancer and inflammation activity [26]. From the present study area, it's clearly evidenced that the usage of aristolochic acid contained plants as a medicine existed previously in Indian subcontinent [28].

Congruently *Nelumbo nucifera* Gaertn also has shown activities like antineurotic (0.851/0.009), antitussive (0.836/0.003) and anti eczematic (0.851/0.010) and these also comparably to the herbalist information obtained from the study area, and the seeds are used in hepatocellular carcinoma [29]. These two inferences from *in silico* prediction, documentation of study data and pertinent literature briefly quoted the correlation between anti-inflammatory plants in cancer and apparently. It supports description in Ayurveda, which cited 5000 years back as inflammation can lead to cancer [10]. Comprehension of the total number of 19 species collected from the study location manifest various bioactivity in the PASS prediction indicated as apoptosis agonist, hepatoprotectant, and insulin promoter other than antineoplastic, which hold desired different probabilities (Table 4). The database of admetSAR is a mechanized free tool which predicts assimilation profiles of drugs as takes after intestinal ingestion, P-glycoprotein substrate and inhibitor, plasma protein restricting correspondingly unique

Table 3
Results obtained from herbalist belongs to the study area.

S. No	Binomial name	Family/ vernacular name	Parts used[a]	Method of preparation	Ailments treated	Administration route[b]	Administration duration	Time require for cure	Total number of citation	UV
1	*Abutilon indicum* (L.) Sweet	Malvaceae/ Thutthi	L	Decoction	Ulcer and tumor in stomach	O	Once a day	60	12	0.60
				Paste	Inflammation and wounds	T	Once a day	48		
2	*Acorus calamus* L.	Acoraceae/ Vasampu	Tu	Paste	Inflammation, wounds, cuts and tumors in skin	T	Once a day	36	9	0.40
3	*Aristolochia bracteolata* Lam.	Aristolochiaceae/ Aaduthinnapaalai	L	Juice	Urinary bladder infections, wounds, inflammations and tumor	O	Two days once	58		
4	*Butea monosperma* (Lam.) Taub.	Fabaceae/Porasu maram	B	Powder	Wounds and inflammation	T	Two times a day	48	6	0.46
					Mixed with milk for ulcer and tumor in stomach	O	Two times a day	60		
5	*Chloroxylon swietenia* DC.	Rutaceae/Ven porinji maram	L	Paste	Inflammation, tumors and wounds	T	Once a day	48	4	0.40
6	*Clematis gouriana* Roxb. ex DC.	Ranunculaceae/ Silankodi	L	Powder	Mixed with curd for inflammation and tumors	T	Twice aday	36	8	0.54
7	*Diospyros Montana* Roxb.	Ebenaceae/ Vakanathi	B	Powder	For inflammation of wounds and tumors	T	Once a day	27	5	0.54
8	*Gmelina arborea* Roxb.	Verbenaceae/ Kumali maram	Wp	Paste	For wounds, inflammation and tumors	T	Once a day	36	3	0.49
9	*Lawsonia inermis* L.	Lythraceae/ Marudhani	L	Powder	For skin infections, inflammation, tumor and wounds	T	Twice a day	48	16	0.63
10	*Leucas aspera* (Willd.) Link	Lamiaceae/ Thumpai chedi	L	Juice	To treat stomach and intestinal ulcers and tumors	O	Twice a day	48	15	0.60
			F	Juice	Mixed with onion juice to treat severe ulceration in stomach		Twice a day	60		
11	*Lycopersicon esculentum* Mill.	Solanaceae/ Thakkali chedi	L	Paste	For inflammation, tumor, burns and skin infections	T	Thrice a day	60	18	0.63
			Se	Paste	Mixed with milk and applied over Skin tumor		Twice a day	48		
12	*Madhuca indica* J. F.Gmel.	Sapotaceae/ Iluppai	B	Decoction	Mixed with honey and used for stomach inflammation and tumor	O	Two days once	36	11	0.66
			B & L	Paste	For skin tumors	T	Once a day	30		
13	*Mallotus philippensis* (Lam.) Müll.Arg.	Euphorbiaceae/ Kurangu manjanathi	B	Extract	For stomach ulceration, inflammation and tumor	O	Two days once	27	9	0.46
14	*Nelumbo nucifera* Gaertn	Nelumbonaceae/ Thamarai	Se	Powder	Mixed with curd to cure stomach ulcer and tumor	O	Twice a day	60	19	0.54
15	*Nyctanthes arbor-tristis* L.	Oleaceae/ Pavilamalli	L	Extract	Mixed with salt for stomach tumor and ulcer	O	Once a day	48	20	0.57
16	*Polyalthia longifolia*(Sonn.) Thwaites	Annonaceae/ Nettilingam	B	Decoction	For intestinal inflammation and tumor	O	Once a ay	48	21	0.60
17	*Sesamum indicum* L.	Pedaliaceae/Ellu chedi	Se	Powder	Mixed with honey for colon infections and tumor	O	Twice a day	48	19	0.54
18	*Sida acuta* Burm. f.	Malvaceae/Vatta thirupi	L	Powder	Mixed with curd to treat skin inflammation	T	Twice a day	27	15	0.43
				Extract	Stomach tumor	O	Once a day	27		
19	*Tribulus terrestris* L.	Zygophyllaceae/ Nerunchi	Se	Decoction	Mixed with salt to cure stomach problems and tumor	O	Twice a day	48	16	0.46
20	*Vitex negundo* L.	Lamiaceae Nocchi	L	Decoction	Stomach inflammation and tumor	O	Two days once	27	14	0.40

[a] B-bark, L-leaf, Se-seed, Fl-flower, Wp-whole plant, Tu-Tuber.
[b] O-oral, T-topical.

kind of digestion as cytochrome substrate, inhibitor, activator and poisonous quality profiles like medication instigated liver damage, mutagenicity, cancer-causing agents [30]. As indicated by the results displayed in Table 4, all the compounds reported from listed plants, demonstrated low toxicity and low carcinogenicity. From the outcomes, all the reported compounds were considered as they can metabolize easily without causing much of problems, retained and transported through human intestinal.

3.4. In silico CLC-Pred cell line cytotoxicity prediction results

A CLC-Pred tool designed to predict the cell line toxicity and an active probability of compounds, a well-known tool in cheminformatics and medicinal chemistry to predict the cell line type and tissue to the respecting tumor type. The prediction was performed for all the 23 selected compounds, which cited as most active in the respective plant species (Table 5). The estimation of results

Table 4
In silico PASS and admetSAR prediction of compounds from documented plants from the study area.

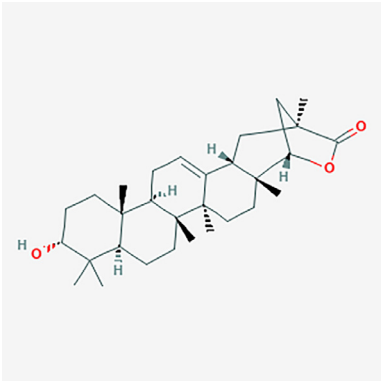
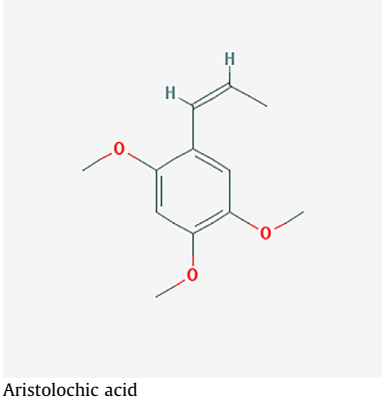
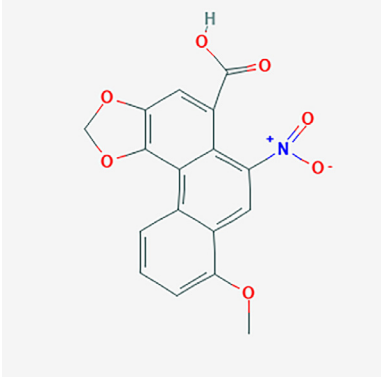
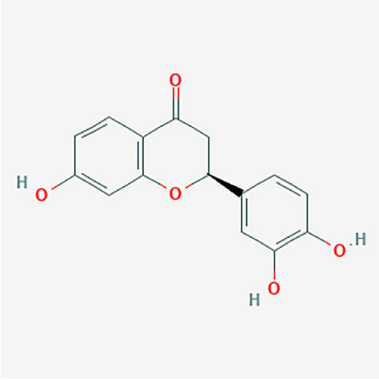
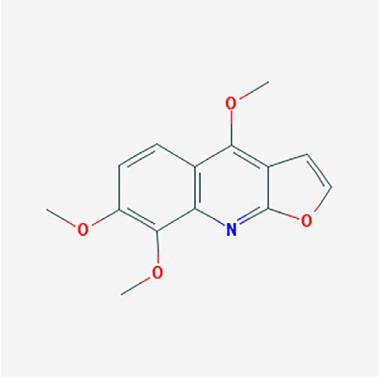
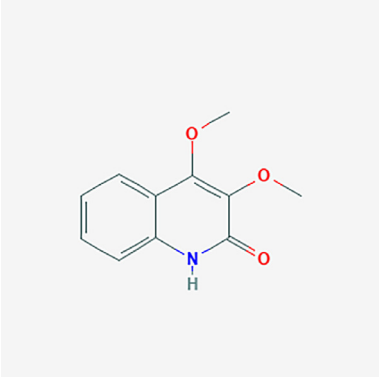
S. no	Plant name	Reported compounds with details	PASS prediction	Pa	Pi	admetSAR prediction		
						A	M	T
1	*Abutilon indicum* (L.) Sweet	Abruslactone A Pubchem ID: 44575701 Molecular weight: 454.695 g/mol Molecular formula: $C_{30}H_{46}O_3$ SMILES:C[C@]12CC[C@H](C([C@@H]1CC[C@@]3([C@@H]2CC=C4[C@]3(CC[C@@]5([C@H]4C[C@]6(C[C@@H]5OC6=O)C)C)C)(C)C)O 	Antineoplastic Apoptosis agonist Insulin promoter Hepatoprotectant Chemopreventive Antineoplastic (lung cancer)	0.928 0.919 0.842 0.811 0.800 0.774	0.005 0.004 0.003 0.004 0.004 0.005	+ +	+ +	+ +
2	*Acorus calamus* L.	Beta-Asarone Pubchem ID: 5281758 Molecular weight: 208.257 g/mol Molecular formula: $C_{12}H_{16}O_3$ SMILES:C/C=C\C1=CC(=C(C=C1OC)OC)OC 	Carminative Apoptosis agonist Antineoplastic	0.905 0.802 0.729	0.008 0.008 0.021	+ +	+ + +	+ +
3	*Aristolochia bracteolata*Lam.	Aristolochic acid Pubchem ID: 2236 Molecular weight: 341.275 g/mol Molecular formula: $C_{17}H_{11}NO_7$ SMILES:COC1=CC=CC2=C3C(=C(C=C21)[N+](=O)[O-])C(=CC4=C3OCO4)C(=O)O 	Antiseptic Respiratory analeptic Apoptosis agonist	0.968 0.828 0.821	0.002 0.007 0.007	+ +	+ + +	+ + +

Table 4 (*continued*)

S. no	Plant name	Reported compounds with details	PASS prediction	Pa	Pi	admetSAR prediction		
						A	M	T
4	*Butea monosperma* (Lam.) Taub.	Butin Pubchem ID: 92775 Molecular weight: 272.256 g/mol Molecular formula: $C_{15}H_{12}O_5$ SMILES:C1[C@H](OC2=C(C1=O)C=CC(=C2)O)C3=CC(=C(C=C3)O)O	Membrane integrity agonist Antimutagenic Cytoprotectant	0.953 0.848 0.796	0.003 0.003 0.002	+ +	+ + +	+ +
								
5	*Chloroxylon swietenia* DC.	Skimmianine Pubchem ID: 6760 Molecular weight: 259.261 g/mol Molecular formula: $C_{14}H_{13}NO_4$ SMILES:COC1=C(C2=C(C=C1)C(=C3C=COC3=N2)OC)OC	Beta glucuronidase inhibitor Antineoplastic	0.790 0.660	0.002 0.033	+ +	+ + +	+ +
								
		Swietenidin B Pubchem ID: 442933 Molecular weight: 205.213 g/mol Molecular formula: $C_{11}H_{11}NO_3$ SMILES:COC1=C(C(=O)NC2=CC=CC=C21)OC	Aspulvinone dimethylallyltransferase inhibitor	0.816	0.028	+ +	+ + +	+ +
								

(*continued on next page*)

Table 4 (*continued*)

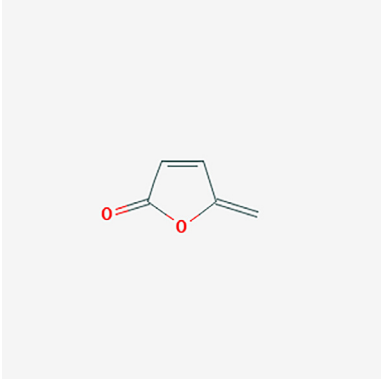
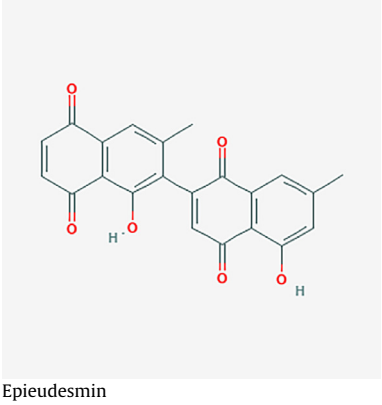
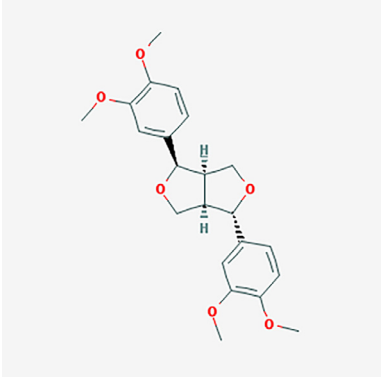
S. no	Plant name	Reported compounds with details	PASS prediction	Pa	Pi	admetSAR prediction		
						A	M	T
6	*Clematis gouriana* Roxb. ex DC.	Protoanemonin Pubchem ID: 66948 Molecular weight: 96.085 g/mol Molecular formula: $C_5H_4O_2$ SMILES:C=C1C=CC(=O)O1 	Antileukemic Antineoplastic	0.919 0.911	0.004 0.005	+ +	+ +	+ +
7	*Diospyros montana* Roxb.	Diospyrin Pubchem ID: 308140 Molecular weight: 374.348 g/mol Molecular formula: $C_{22}H_{14}O_6$ SMILES:CC1=CC(=C2C(=C1)C(=O)C(=CC2=O)C3=C(C=C4C(=O)C=CC(=O)C4=C3O)C)O 	Antiseptic Antineoplastic Antimutagenic	0.860 0.852 0.783	0.004 0.007 0.004	+ + +	+ + +	+
8	*Gmelina arborea* Roxb.	Epieudesmin Pubchem ID: 7000209 Molecular weight: 386.444 g/mol Molecular formula: $C_{22}H_{26}O_6$ SMILES:COC1=C(C=C(C=C1)[C@H]2[C@H]3CO[C@@H]([C@H]3CO2)C4=CC(=C(C=C4)OC)OC)OC 	Antineoplastic Cardiovascular analeptic	0.807 0.725	0.011 0.006	+ + +	+ +	+

Table 4 (*continued*)

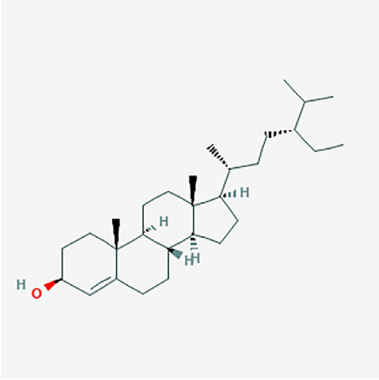
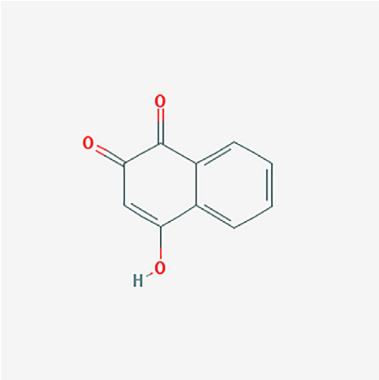
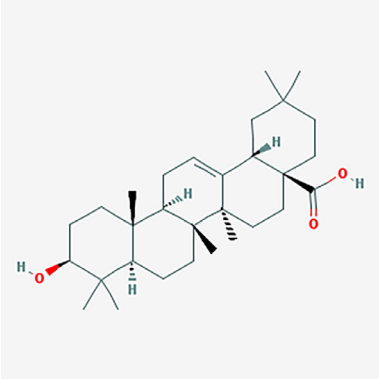
S. no	Plant name	Reported compounds with details	PASS prediction	Pa	Pi	admetSAR prediction		
						A	M	T
9	*Lawsonia inermis* L.	Lawsaritol Pubchem ID: 14890646 Molecular weight: 414.718 g/mol Molecular formula: $C_{29}H_{50}O$ SMILES:CC[C@H](CC[C@@H](C)[C@H]1CC[C@@H]2[C@@]1(CC[C@H]3[C@H]2CCC4=C[C@H](CC[C@]34C)O)C)C(C)C	Antihypercholesterolemic Chemopreventive Antieczematic	0.971 0.810 0.806	0.002 0.004 0.017	+ +	+ +	+
								
		Lawsone Pubchem ID: 6755 Molecular weight: 174.155 g/mol Molecular formula: $C_{10}H_6O_3$ SMILES:C1=CC=C2C(=C1)C(=CC(=O)C2=O)O	Vasoprotector Antimutagenic Antineoplastic	0.821 0.805 0.777	0.004 0.004 0.015	+ + +	+ +	+
								
10	*Leucas aspera* (Willd.) Link	Oleanolic acid Pubchem ID: 10494 Molecular weight: 456.711 g/mol Molecular formula: $C_{30}H_{48}O_3$ SMILES:C[C@]12CC[C@@H](C([C@@H]1CC[C@@]3([C@@H]2CC=C4[C@]3(CC[C@@]5([C@H]4CC(CC5)(C)C)C(=O)O)C)(C)C)O	Insulin promoter Hepatoprotectant Chemopreventive Antinociceptive Antineoplastic	0.987 0.961 0.937 0.985 0.877	0.001 0.001 0.002 0.001 0.005	+ +	+ + +	+ +
								

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Table 4 (*continued*)

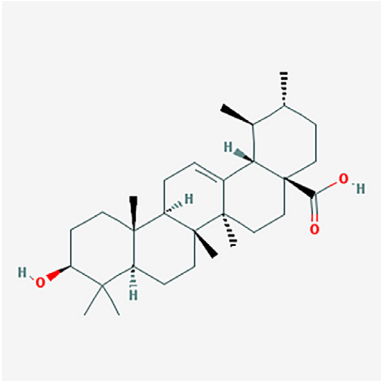
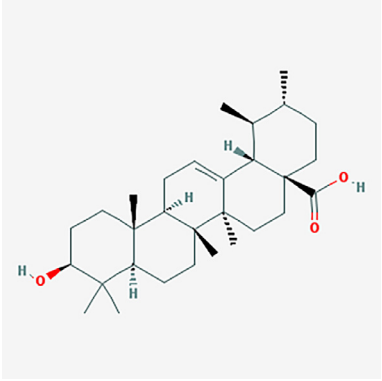
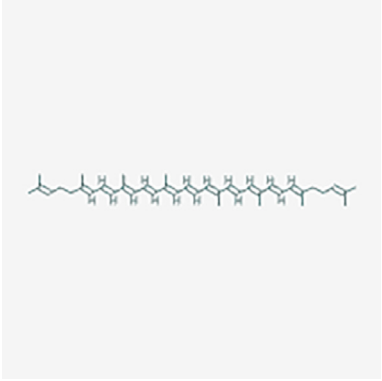
S. no	Plant name	Reported compounds with details	PASS prediction	Pa	Pi	admetSAR prediction		
						A	M	T
		Ursolic Acid Pubchem ID: 64945 Molecular weight: 456.711 g/mol Molecular formula: $C_{30}H_{48}O_3$ SMILES:C[C@@H]1CC[C@@]2(CC[C@@]3(C(=CC[C@H]4[C@]3(CC[C@@H]5[C@@]4(CC[C@@H](C5(C)C)O)C)C)[C@@H]2[C@H]1C)C)C(=O)O	Insulin promoter Hepatoprotectant Chemopreventive Antiprotozoal	0.970 0.961 0.929 0.915	0.001 0.001 0.002 0.003	+ +	+ + +	+
								
11	*Lycopersicon esculentum* Mill.	Lycopene Pubchem ID: 446925 Molecular weight: 536.888 g/mol Molecular formula: $C_{40}H_{56}$ SMILES:CC(=CCC/C(=C/C=C/C(=C/C=C/C(=C/C=C/C=C(/C=C/C=C(/C=C/C=C(/CCC=C(C)C)\C)\C)\C)/C)/C)C	Apoptosis agonist Antineoplastic Antioxidant	0.934 0.905 0.848	0.004 0.005 0.003	+ +	+ +	+
								
12	*Madhuca indica* J. F.Gmel.	Betulinic acid Pubchem ID: 64971 Molecular weight: 456.711 g/mol Molecular formula: $C_{30}H_{48}O_3$ SMILES:CC(=C)[C@@H]1CC[C@]2([C@H]1[C@H]3CC[C@@H]4[C@]5(CC[C@@H](C([C@@H]5CC[C@]4([C@@]3(CC2)C)C)(C)C)O)C)C(=O)O	Hepatoprotectant Antineoplastic Antiprotozoal Chemopreventive Antineoplastic (melanoma)	0.952 0.925 0.923 0.835 0.825	0.002 0.005 0.003 0.003 0.003	+ +	+ +	+
								

Table 4 (*continued*)

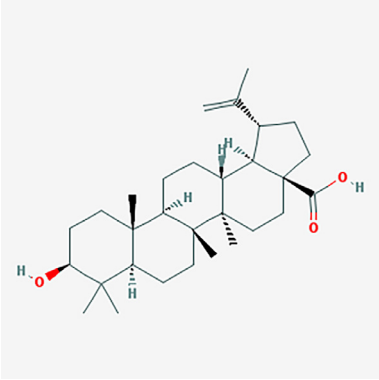
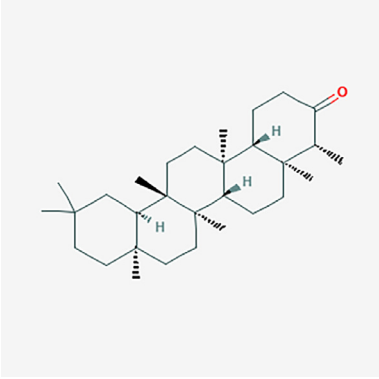
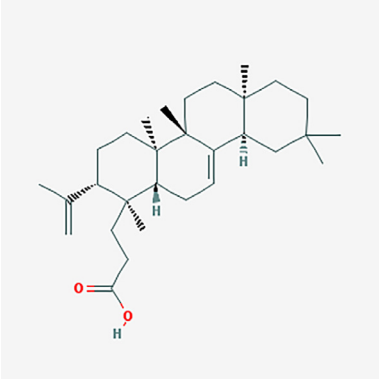
S. no	Plant name	Reported compounds with details	PASS prediction	Pa	Pi	admetSAR prediction		
						A	M	T
13	*Mallotus philippensis* (Lam.) Müll.Arg.	Friedelin Pubchem ID: 91472 Molecular weight: 426.729 g/mol Molecular formula: $C_{30}H_{50}O$ SMILES:C[C@H]1C(=O)CC[C@@H]2[C@@]1(CC[C@H]3[C@]2(CC[C@@]4([C@@]3(CC[C@@]5([C@H]4CC(CC5)(C)C)C)C)C)C)C	Apoptosis agonist Antineoplastic	0.871 0.850	0.005 0.007	+ + +	+ + +	+
								
14	*Nelumbo nucifera* Gaertn	Nuciferine Pubchem ID: 10146 Molecular weight: 295.382 g/mol Molecular formula: $C_{19}H_{21}NO_2$ SMILES:CN1CCC2=CC(=C(C3=C2[C@H]1CC4=CC=CC=C43)OC)OC	Antineurotic Antitussive Antieczematic	0.851 0.836 0.851	0.009 0.003 0.010	+ + +	+ + +	+
								
15	*Nyctanthes arbor-tristis* L.	Nyctanthic acid Pubchem ID: 12313631 Molecular weight: 440.712 g/mol Molecular formula: $C_{30}H_{48}O_2$ SMILES:CC(=C)[C@@H]1CC[C@@]2([C@@H]([C@@]1(C)CCC(=O)O)CC=C3[C@]2(CC[C@@]4([C@H]3CC(CC4)(C)C)C)C)C	Hepatoprotectant Insulin promoter Antineoplastic Chemopreventive	0.897 0.838 0.826 0.814	0.002 0.004 0.009 0.004	+ + +	+ +	+
								

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Table 4 (*continued*)

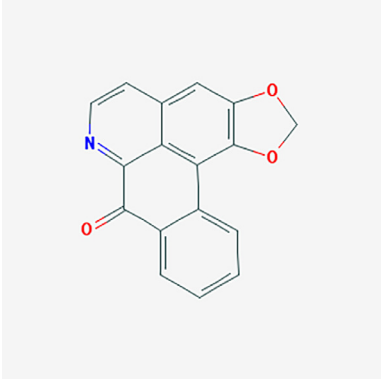
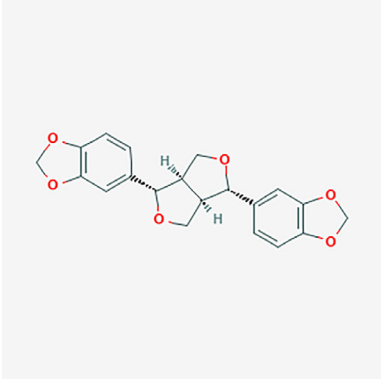
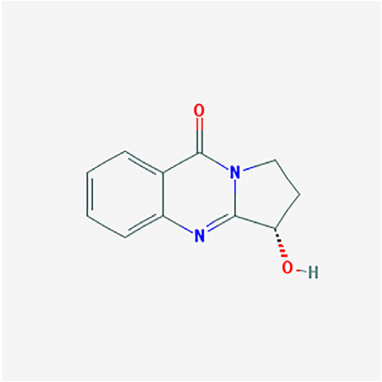
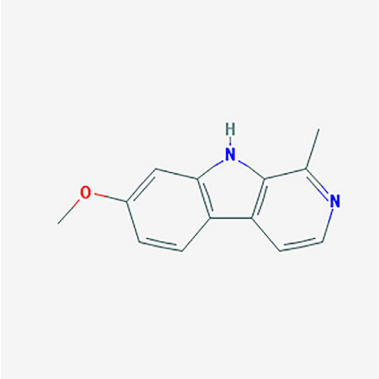
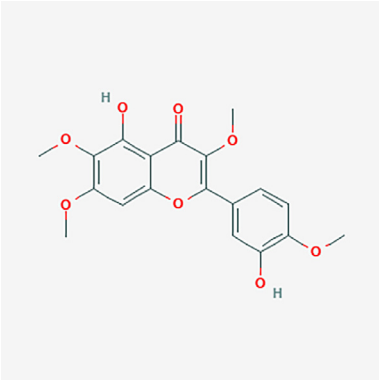
S. no	Plant name	Reported compounds with details	PASS prediction	Pa	Pi	admetSAR prediction		
						A	M	T
16	*Polyalthia longifolia* (Sonn.) Thwaites	Liriodenine Pubchem ID: 10144 Molecular weight: 275.263 g/mol Molecular formula: $C_{17}H_9NO_3$ SMILES:C1OC2=C(O1)C3=C4C(=C2)C=CN=C4C(=O)C5=CC=CC=C53	Neurotransmitter uptake inhibitor Antineoplastic Antineoplastic (colorectal cancer)	0.888 0.786 0.688	0.002 0.014 0.005	+ +	+ + +	+
								
17	*Sesamum indicum* L.	Sesamin Pubchem ID: 72307 Molecular weight: 354.358 g/mol Molecular formula: $C_{20}H_{18}O_6$ SMILES:C1[C@H]2[C@H](CO[C@@H]2C3=CC4=C(C=C3)OCO4)[C@H](O1)C5=CC6=C(C=C5)OCO6	Membrane integrity agonist Antineoplastic Carminative	0.931 0.797 0.761	0.005 0.012 0.004	+ + +	+ +	+
								
18	*Sida acuta* Burm.f.	Vasicinone Pubchem ID: 442935 Molecular weight: 202.213 g/mol Molecular formula: $C_{11}H_{10}N_2O_2$ SMILES:C1CN2C(=NC3=CC=CC=C3C2=O)[C@H]1O	Antihypoxic Antineoplastic (multiple myeloma)	0.744 0.564	0.005 0.005	+ +	+ +	+ +
								

Table 4 (*continued*)

S. no	Plant name	Reported compounds with details	PASS prediction	Pa	Pi	admetSAR prediction		
						A	M	T
19	*Tribulus terrestris* L.	Harmine Pubchem ID: 5280953 Molecular weight: 212.252 g/mol Molecular formula: $C_{13}H_{12}N_2O$ SMILES:CC1=NC=CC2=C1NC3=C2C=CC(=C3)OC 	Lysase inhibitor Preneoplastic conditions treatment	0.681 0.628	0.026 0.019	+ +	+ +	+
20	*Vitex negundo* L.	Vitexicarpin Pubchem ID: 5315263 Molecular weight: 374.345 g/mol Molecular formula: $C_{19}H_{18}O_8$ SMILES:COC1=C(C=C(C=C1)C2=C(C(=O)C3=C(C(=C(C=C3O2)OC)OC)O)OC)O 	Antimutagenic Apoptosis agonist Antineoplastic	0.928 0.895 0.832	0.002 0.004 0.008	+ +	+ +	+

SMILES: Simplified molecular-input line-entry system; Pa: Probable activity, Pi: Probable inactivity; A: Adsorption; M: Metabolism; T: Toxicity.

presented in a Pa values, which is >0.5 are probably more active with the predicted cancer cell line. From the 20 plants 23 of compounds specifically selected and executed for cytotoxicity activity prediction in different cell lines by employing CLC-Pred tool. Almost all the plants showed aspirated outcome and barely three compounds displayed negative results those compounds are aristolochic acid (*Aristolochia bracteolata* Lam.), skimmianine (*Chloroxylon swietenia* DC.) and vitexicarpin (*Vitex negundo* L). The aristolochic acid CLC-Pred negative result greatly concurs in the result of PASS, but it is rationally used for tumor contradict vitexicarpin showed positive correlation with both PASS prediction and study result (Tables 4 and 5).

The maximum number of different cell line prediction were collected and tabulated with respective cancer type, probability, and type of cell. The compounds oleanolic acid and ursolic acid from *Leucas aspera* (Willd.) Link showed significant cytotoxity against stomach adenocarcinoma (0.820/MKN-74), thyroid carcinoma (0.592/8505C), upper aero digestive tract carcinoma (0.505/FaDu), pancreas adenocarcinoma (0.504/ASPC-1), and stomach carcinoma (0.502/MKN-7) with significant Pa values (Table 5). Likewise, sesamin of *Sesamum indicum* L. renders strong activity against lung carcinoma (0.760/A549), central nervous system oligodendroglioma (0.687/Hs683), central nervous system glioblastoma (0.522/SF-295), colon adenocarcinoma (0.506/HCC2998) and stomach adenocarcinoma (0.505/MKN-74) besides vasicinone from *Sida acuta* Burm.f. showed cytotoxicity against central nervous system oligodendroglioma (0.562/Hs683), Pleura mesothelioma (0.588/NCI-H2052) and lung carcinoma (0.530/PC-6). The other remaining compounds from the reported plants, *Madhuca indica* J.F.Gmel. (betulinic acid) (4), *Lawsonia inermis* L. (lawsaritol, Lawsone) (4), *Abutilon indicum* (L.) Sweet (Abruslactone A) (3), *Lycopersicon esculentum* Mill. (lycopene) (3), *Polyalthia longifolia* (Sonn.) Thwaites (liriodenine) (3), *Chloroxylon swietenia* DC (skimmianine, Swietenidin B) (2), *Diospyros montana* Roxb. (Diospyrin) (2), *Gmelina arborea* Roxb. (epieudesmin) (2) and *Mallotus philippensis* (Lam.) Müll.Arg. (friedelin) (2) showed cytotoxicity against various cell lines respective of their affecting tissue. *Nyctanthes arbor-tristis* L. (nyctanthic acid) inversely *Butea monosperma* (butin), *Nelumbo nucifera* Gaertn (Nuciferine) *Tribulus terrestris* L. (harmine) predicted with single cell lines cytotoxicity activity (Table 5).

Tribulus terrestris L. displayed only lung adenocarcinoma cytotoxicity whereas present study and literature survey matches for hepatocellular carcinoma [31] comparatively *Nelumbo nucifera* Gaertn. mentioned to have traditionally used for inflammation

Table 5
In silico CLC-Pred cell line cytotoxicity prediction of documented plants from the study area.

Plant name	Compounds[a]	Cell line	Cell line model type	Affecting parts	Tumor type	Pa	Pi
Abutilon indicum (L.) Sweet	Abruslactone A	MKN-74	Stomach adenocarcinoma cells	Stomach	Adenocarcinoma	0.728	0.004
		MKN-28	Gastric epithelial carcinoma cells	Stomach	Carcinoma	0.513	0.016
		MKN-7	Gastric carcinoma cells	Stomach	Carcinoma	0.522	0.034
Acorus calamus L.	Beta-Asarone	TE-671	Human Rhabdomyosarcoma cell line	Muscle	Sarcoma	0.671	0.005
Butea monosperma	Butin	PC-6	Small cell lung carcinoma cells	Lung	Carcinoma	0.519	0.023
Chloroxylon swietenia DC	Skimmianine	TE-671	Human Rhabdomyosarcoma cell line	Muscle	Sarcoma	0.551	0.023
	Swietenidin B	HS 683	Oligodendroglioma cells	Central nervous system	Oligodendroglioma	0.505	0.014
Clematis gouriana Roxb. ex DC.	Protoanemonin	TE-671	Human Rhabdomyosarcoma cell line	Muscle	Sarcoma	0.682	0.005
		NALM-6	Adult B acute lymphoblastic leukemia cells	Haematopoietic and lymphoid tissue	Leukemia	0.545	0.003
Diospyros Montana Roxb.	Diospyrin	HOP-18	Non-small cell lung carcinoma cells	Lung	Carcinoma	0.627	0.003
		NC-H2052	Epithelioid mesothelioma cells	Pleura	Mesothelioma	0.557	0.096
Gmelina arborea Roxb.	Epieudesmin	A549	Lung carcinoma cells	Lung	Carcinoma	0.575	0.046
		PC-6	Small cell lung carcinoma cells	Lung	Carcinoma	0.534	0.022
Lawsonia inermis L.	Lawsaritol	MKN-74	Stomach adenocarcinoma cells	Stomach	Adenocarcinoma	0.682	0.006
	Lawsone	MKN-7	Gastric carcinoma cells	Stomach	Carcinoma	0.548	0.023
		TE-671	Human Rhabdomyosarcoma cell line	Muscle	Sarcoma	0.634	0.009
		NC-H2052	Epithelioid mesothelioma cells	Pleura	Mesothelioma	0.501	0.144
Leucas aspera (Willd.) Link	Oleanolic acid	MKN-74	Stomach adenocarcinoma cells	Stomach	Adenocarcinoma	0.820	0.002
	Ursolic acid	8505C	Thyroid gland undifferentiated (anaplastic) carcinoma cells	Thyroid	Carcinoma	0.592	0.004
		FaDu	Hypopharyngeal squamous carcinoma cells	Upper aerodigestive tract	Carcinoma	0.505	0.007
		MKN-74	Stomach adenocarcinoma cells	Stomach	Adenocarcinoma	0.756	0.003
		ASPC-1	Pancreatic ductal adenocarcinoma cells	Pancreas	Adenocarcinoma	0.504	0.004
		MKN-7	Gastric carcinoma cells	Stomach	Carcinoma	0.502	0.042
Lycopersicon esculentum Mill.	Lycopene	TE-671	Human Rhabdomyosarcoma cell line	Muscle	Sarcoma	0.803	0.003
		LOX	Breast carcinoma cells	Breast	Carcinoma	0.695	0.018
		IMVI	Melanoma cells	Skin	Melanoma	0.529	0.015
		MKN-74	Gastric carcinoma cells	Stomach	Carcinoma	0.575	0.019
Madhuca indica J.F.Gmel.	Betulinic acid	FaDu	Hypopharyngeal squamous carcinoma cells	Upper aerodigestive tract	Carcinoma	0.794	0.003
		8505C	Thyroid gland undifferentiated (anaplastic) carcinoma cells	Thyroid	Carcinoma	0.724	0.003
		MKN-74	Stomach adenocarcinoma cells	Stomach	Adenocarcinoma	0.654	0.008
		SK-MEL-2	Melanoma cells	Skin	Melanoma	0.560	0.013
Mallotus philippensis (Lam.) Müll.Arg.	Friedelin	MKN-74	Stomach adenocarcinoma cells	Stomach	Adenocarcinoma	0.614	0.013
		H9	T-lymphoid cells	Haematopoietic and lymphoid tissue	Lymphoma	0.507	0.006
Nelumbo nucifera Gaertn	Nuciferine	A549	Lung carcinoma cells	Lung	Carcinoma	0.502	0.060
Nyctanthes arbor-tristis L.	Nyctanthic acid	MKN-74	Stomach adenocarcinoma cells	Stomach	Adenocarcinoma	0.597	0.015
		FaDu	Hypopharyngeal squamous carcinoma cells	Upper aerodigestive tract	Carcinoma	0.521	0.006
Polyalthia longifolia (Sonn.) Thwaites	Liriodenine	A549	Lung carcinoma cells	Lung	Carcinoma	0.675	0.027
		HCT-15	Colon adenocarcinoma cells	Large intestine	Adenocarcinoma	0.613	0.010
		SF-268	Glioblastoma cells	Brain	Glioblastoma	0.529	0.017
Sesamum indicum L.	Sesamin	A549	Lung carcinoma cells	Lung	Carcinoma	0.760	0.016
		Hs 683	Oligodendroglioma cells	Central nervous system	Oligodendroglioma	0.687	0.004
		SF-295	Glioblastoma cells	Central nervous system	Glioblastoma	0.522	0.016
		HCC 2998	Colon adenocarcinoma cells	Colon	Adenocarcinoma	0.506	0.023
		MKN-74	Stomach adenocarcinoma cells	Stomach	Adenocarcinoma	0.505	0.036
Sida acuta Burm.f.	Vasicinone	Hs 683	Oligodendroglioma cells	Central nervous system	Oligodendroglioma	0.562	0.008
		NCI-H2052	Epithelioid mesothelioma cells	Pleura	Mesothelioma	0.588	0.076
		PC-6	Small cell lung carcinoma cells	Lung	Carcinoma	0.530	0.022
		MSTO-211H	Pleural mesothelioma cells	Pleura	Mesothelioma	0.501	0.114
Tribulus terrestris L.	Harmine	SK-LU-1	Lung adenocarcinoma	Lung	Adenocarcinoma	0.508	0.069

[a] The compounds details were given in Table 4; Pa: Probable activity, Pi: Probable inactivity.

and cancer it greatly resembles with present study [32]. Likewise, *Butea monosperma* reported for its traditional usage as the anti-inflammatory and strong anti-cancer against hepatoma cells [33]. Above assertion grant adequate knowledge about the interconnection between anti-inflammatory plants with anti- cancer properties, and it authenticates undoubtedly Indian tradition of medicine have sufficient skills in treating cancer-related ailments and other disparate afflictions as evinced in "Ayurveda."

4. Conclusion

Studies on ethno medicinal anti-inflammatory and wound healing was abundant all over the world beyond particular attention paid to Indian ethnic societies, which have age-old therapeutic practices and guidelines for prescription medicaments by herbalist and traditional healers. The present study documented about 20 ethno medicinal plants that are utilized as anti-inflammatory,

wound healing agents and also in the treatment of cancer based on the traditional reports, particularly *Nyctanthes arbor-tristis*, *Butea monosperma; Tribulus terrestris* predicted cytotoxicity activity significantly correlated with the literature survey. The selected compounds from reported plants revealed significant anticancer activity in CLC-Pred prediction and PASS tools. This study entirely draws the appreciable output on the relationship of anti-inflammatory plants in cancer and moreover, the *in silico* studies assessed extremely the presence of anticancer activity. This study showed the possibility to correlate ethno pharmacological therapies to develop new pharmaceutical drugs thus can accelerate the interpretative analysis of the ethnic anti-inflammatory plants in the development of anti-cancerous drugs.

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