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

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A B S T R A C T

The present study was designed to explore ethnopharmacological anti-inflammatory plants in the anticancer 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 medicines 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
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 km² (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.

\[ UV = \sum_{i=1}^{N} UR/N \]

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 or 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 cytoxicity 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
(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. Using 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
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 bracteolata* 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 bracteolata* 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 eczematous (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, hepatoprotector, 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 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          | 6    | 2      |
| 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                     | Karpai katti                        |
| 3       | Chronic inflammation             | Vayitrupun katti                    |
| 4       | Inflammation                     | Udaleritcal                         |
| 5       | Burns                            | Theekkaayam                         |
| 6       | Wounds                           | Kaayam                              |
| 8       | Mouth ulcer                      | Vaippun                             |
| 9       | Stomach ache                     | Vayitrupali                         |
| 10      | Stomach ulcer                    | Vayitrupun                          |

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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 3
Results obtained from herbalist belongs to the study area.

| S. No | Binomial name family/ vernacular name | Parts usedb | Method of preparation | Ailments treated | Administration routea | Administration duration | Time require for cure | Total number of citation |
|-------|-------------------------------------|-------------|-----------------------|------------------|----------------------|------------------------|------------------------|---------------------------|
| 1     | Abutilon indicum (L.) Sweet         | L           | Decoction             | Ulcer and tumor in stomach Inflammation and wounds | O                    | Once a day             | 60                     | 12                        | 0.60                      |
| 2     | Acorus calamus L.                   | Tu          | Paste                 | Inflammation, wounds, cuts and tumors in skin | T                    | Once a day             | 48                     | 9                         | 0.40                      |
| 3     | Aristolochia bracteolata Lam.       | L           | Juice                 | Urinary bladder infections, wounds, inflammations and tumor | O                    | Two days once          | 58                     |                           |                           |
| 4     | Butea monosperma (Lam.) Taub.       | B           | Powder                | Wounds and inflammation | T                    | Two times a day        | 48                     | 6                         | 0.46                      |
| 5     | Chloroxylon swietenia DC.           | L           | Paste                 | Mixed with milk for ulcer and tumor in stomach | T                    | Once a day             | 48                     | 4                         | 0.40                      |
| 6     | Clematis gouranii Roxb. ex DC.      | L           | Powder                | Mixed with curd for inflammation and tumors | T                    | Twice a day             | 36                     | 8                         | 0.54                      |
| 7     | Diospyros montana Roxb.             | B           | Powder                | For inflammation of wounds and tumors | T                    | Once a day             | 27                     | 5                         | 0.54                      |
| 8     | Gnetum arbor-saxatilis L.           | Wp          | Paste                 | For wounds, inflammation and tumors | T                    | Once a day             | 36                     | 3                         | 0.49                      |
| 9     | Lawsonia inermis L.                 | L           | Powder                | For skin infections, inflammation, tumor and wounds | T                    | Twice a day             | 48                     | 16                        | 0.63                      |
| 10    | Leucas aspera (Wild.) Link          | L           | Juice                 | To treat stomach and intestinal ulcers and tumors Mixed with onion juice to treat severe ulceration in stomach | O                    | Twice a day             | 48                     | 15                        | 0.60                      |
| 11    | Lycopersicon esculentum Mill.       | L           | Paste                 | For inflammation, tumor, burns and skin infections Mixed with milk and applied over Skin | T                    | Thrice a day             | 60                     | 18                        | 0.63                      |
| 12    | Madhuca indica J. P.Gmel.           | B           | Decoction             | Mixed with honey and used for stomach inflammation and tumor | O                    | Two days once          | 36                     | 11                        | 0.66                      |
| 13    | Mallotus philippensis (Lam.) Müll.Arg. | B & L       | Paste Extract         | For skin tumors For stomach ulceration, inflammation and tumor | T                    | Once a day             | 30                     | 9                         | 0.46                      |
| 14    | Nelumbo nucifera Gaertn             | Se          | Powder                | Mixed with curd to cure stomach ulcer and tumor | O                    | Twice a day             | 60                     | 19                        | 0.54                      |
| 15    | Nymphaea alba L.                    | L           | Extract               | Mixed with salt for stomach and tumor | O                    | Once a day             | 48                     | 20                        | 0.57                      |
| 16    | Polyalthia longifolia(Somn.) Thwaites resinus L. | B           | Decoction             | For intestinal inflammation and tumor | O                    | Once a day             | 48                     | 21                        | 0.60                      |
| 17    | Sesamum indicum L.                  | Se          | Powder                | Mixed with honey for colon infections and tumor | O                    | Twice a day             | 48                     | 19                        | 0.54                      |
| 18    | Sida acuta Burm. f.                 | L           | Powder                | Mixed with curd to treat skin inflammation | T                    | Twice a day             | 27                     | 15                        | 0.43                      |
| 19    | Tribulus terrestris L.              | Se          | Extract Decoction     | Mixed with salt to cure stomach problems and tumor Stomach inflammation and tumor | O                    | Twice a day             | 27                     | 16                        | 0.46                      |
| 20    | Vitex negundo L.                    | 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.
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 |
|-------|------------|---------------------------------|----------------|----|----|---------------------|
| 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\[\@\]1CC\[C\[\@\]H\]\(\text{\[[@\]O}\)C\]C\]C\]C\]C\]O | Antineoplastic 0.928 0.005 + + + | Apoptosis agonist 0.919 0.004 + + + | Insulin promoter 0.842 0.003 | Hepatoprotectant 0.811 0.004 | Chemopreventive 0.800 0.004 | Antineoplastic (lung cancer) 0.774 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\[\@\]CC\[\@\]CC\[\@\]OC\]OC | Carminative 0.905 0.008 + + + | Apoptosis agonist 0.802 0.008 + + + | Antineoplastic 0.729 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\[\@\]CC\[\@\]C\[\@\]C\[\@\]OC\]OC | Antiseptic 0.968 0.002 + + + | Respiratory analeptic 0.828 0.007 + + + | Apoptosis agonist 0.821 0.007 | | |
Table 4 (continued)

| S. no | Plant name                      | Reported compounds with details                                      | PASS prediction | Pa   | Pt   | admetSAR prediction |
|-------|---------------------------------|-----------------------------------------------------------------------|-----------------|------|------|---------------------|
| 4     | *Butea monosperma* (Lam.) Taub. | Butin                                                                 | Membrane integrity 0.953 0.003 | +   | +   | +                   |
|       |                                 | Pubchem ID: 92775                                                     | agonist          +   |     |     | +                   |
|       |                                 | Molecular weight: 272.256 g/mol                                       | Antimutagenic    0.848 0.003 | +   |     | +                   |
|       |                                 | Molecular formula: C₁₅H₁₂O₅ SMILES:C1(C=O)C1=O=C(C=O)C(C=O)C(C=O)C(C1=C3)O | Cytoprotectant   0.796 0.002   |     |     | +                   |
|       |                                 |                                                                         |                 |     |     |                     |
| 5     | *Chloroxylon swietenia* DC.     | Skimmianine                                                            | Beta glucuronidase inhibitor 0.790 0.002 | +   | +   | +                   |
|       |                                 | Pubchem ID: 6760                                                      | Antineoplastic   0.660 0.033   | +   |     | +                   |
|       |                                 | Molecular weight: 259.261 g/mol                                       |                 |     |     |                     |
|       |                                 | Molecular formula: C₁₄H₁₃NO₄ SMILES:COC1=C(C=O)C1=C(C=O)C(C=O)C(C=O)C(C3=C(C=O)C3=O) |                 |     |     |                     |
|       |                                 |                                                                         |                 |     |     |                     |
|       |                                 | Swietenidin B                                                         | Aspulvinone dimethylallyltransferase inhibitor 0.816 0.028 | +   | +   | +                   |
|       |                                 | Pubchem ID: 442933                                                    |                 |     |     |                     |
|       |                                 | Molecular weight: 205.213 g/mol                                       |                 |     |     |                     |
|       |                                 | Molecular formula: C₁₁H₁₁NO₃ SMILES:COC1=C(C=O)C1=C(C=O)C(C=O)C(C1=C2)=C |                 |     |     |                     |

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Table 4 (continued)

| S. no | Plant name                  | Reported compounds with details | PASS prediction | Pa   | Pi   | admetSAR prediction |
|-------|-----------------------------|---------------------------------|----------------|------|------|---------------------|
|       |                             |                                  | Antileukemic   | 0.919| 0.004| + + +              |
| 6     | Clematis gouriana Roxb. ex DC. | Protoanemonin                    | Antineoplastic | 0.911| 0.005| + + +              |
|       |                             | Pubchem ID: 66948                |                |      |      |                     |
|       |                             | Molecular weight: 96.085 g/mol   |                |      |      |                     |
|       |                             | Molecular formula: C₅H₄O₂         |                |      |      |                     |
|       |                             | SMILES: C@C@C(C(O)O)O1           |                |      |      |                     |
| 7     | Diospyros montana Roxb.     | Diospyrin                        | Antiseptic     | 0.860| 0.004| + + +              |
|       |                             | Pubchem ID: 308140               | Antineoplastic | 0.852| 0.007| + +                 |
|       |                             | Molecular weight: 374.348 g/mol  | Antimutagenic  | 0.783| 0.004| + +                 |
|       |                             | Molecular formula: C₂₂H₁₄O₆      |                |      |      |                     |
|       |                             | SMILES: | | | | | |
| 373x* |                             |                                 |                |      |      |                     |
| 8     | Gmelina arborea Roxb.      | Epidesmin                        | Antineoplastic | 0.807| 0.011| + + +              |
|       |                             | Pubchem ID: 7000209              | Cardiovascular analeptic | 0.725| 0.006| + +                 |
|       |                             | Molecular weight: 386.444 g/mol  |                |      |      |                     |
|       |                             | Molecular formula: C₂₂H₂₆O₆      |                |      |      |                     |
|       |                             | SMILES: COC1=C(C=C=C1)[C@H]₂[C@H]₂COC[O@H]₂[C@H]₂COCX₄=CC(C=C=C4)OCOCOCOC | | | | |
| S. no | Plant name | Reported compounds with details | PASS prediction | Pa | Pi | admetSAR prediction |
|------|------------|--------------------------------|----------------|----|----|---------------------|
| 9    | *Lawsonia inermis* L. | Lawsaritol | Antihypercholesterolemic | 0.971 | 0.002 | + + + |
|      |            | Pubchem ID: 14890646 | Chemopreventive | 0.810 | 0.004 | + |
|      |            | Molecular weight: 414.718 g/mol | Antieczematic | 0.806 | 0.017 | + |
|      |            | Molecular formula: $C_{29}H_{50}O$ | | | | |
|      |            | SMILES: | | | | |
|      |            | $CC\{C\@H\}(CC\{C\@H\}(C)\{C\@H\}1CC\{C\@H\}2(C\{C\@H\}| | | |
|      |            | $\{C\@H\}|CC\{C\@H\}3|C\@H|2CCC4=C|C\@H|CC\{C\@H\}|34C\{O\}C|C\{C\}C | | |
|      |            | Lawsone | Vasoprotector | 0.821 | 0.004 | + + + |
|      |            | Pubchem ID: 6755 | Antimutagenic | 0.805 | 0.004 | + |
|      |            | Molecular weight: 174.155 g/mol | Antineoplastic | 0.777 | 0.015 | + |
|      |            | Molecular formula: $C_{10}H_{6}O_{3}$ | | | | |
|      |            | SMILES: | | | | |
|      |            | $C1\{C\@H\}CC\{C\@H\}(O)C1\{O\}O$ | | | | |
| 10   | *Leucas aspera* (Willd.) Link | Oleanolic acid | Insulin promoter | 0.987 | 0.001 | + + + |
|      |            | Pubchem ID: 10494 | Hepatoprotectant | 0.961 | 0.001 | + + + |
|      |            | Molecular weight: 456.711 g/mol | Chemopreventive | 0.937 | 0.002 | + |
|      |            | Molecular formula: $C_{30}H_{48}O_{3}$ | Antinociceptive | 0.985 | 0.001 | + |
|      |            | SMILES: | | | | |
|      |            | $C\{C\@H\}12CC\{C\@H\}(C\{C\@H\}|CC\{C\@H\}|3\{C\@H\}|2CC=31CC\{C\@H\}=O|O|C\{C\}3\{C\}O | | |
|      |            | $(\{C\@H\}|CC=4|C\{O\}3\{C\}3|CC\{C\@H\}|5\{C\@H\}|4CC(CS)(\{C\}|C\{O\}O)|O|C\{C\}3\{C\}O | | |

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Table 4 (continued)

| S. no | Plant name                  | Reported compounds with details | PASS prediction | Pa   | Pi   | admetSAR prediction |
|-------|-----------------------------|---------------------------------|----------------|------|------|---------------------|
|       |                             |                                 |                |      |      |                     |
|       |                             |                                 |                |      |      | A      | M     | Y     |
|       |                             |                                 |                |      |      |        |       |       |
| 11    | *Lycopersicon esculentum* Mill. | Lycopene                        | Apoptosis agonist | 0.934 | 0.004 | +     | +     | +     |
|       |                             |                                 | Antineoplastic  | 0.905 | 0.005 | +     | +     |       |
|       |                             |                                 | Antioxidant     | 0.848 | 0.003 |       |       |       |
| 12    | *Madhuca indica* J. F.Gmel. | Betulinic acid                  | Hepatoprotectant | 0.952 | 0.002 | +     | +     | +     |
|       |                             |                                 | Antineoplastic  | 0.925 | 0.005 | +     | +     |       |
|       |                             |                                 | Antiprotozoal   | 0.923 | 0.003 | +     |       |       |
|       |                             |                                 | Chemopreventive | 0.835 | 0.003 |       |       |       |
|       |                             |                                 | Antineoplastic  (melanoma) | 0.825 | 0.003 |       |       |       |
Table 4 (continued)

| S. no | Plant name | Reported compounds with details | PASS prediction | Pa | Pi | admetSAR prediction |
|-------|------------|--------------------------------|----------------|----|----|---------------------|
| 13    | Mallotus philippensis (Lam.) Müll.Arg. | Friedelin | Apoptosis agonist 0.871 0.005 + + + | Antineoplastic 0.850 0.007 + + + | |
|       |            | Pubchem ID: 91472 | Molecular weight: 426.729 g/mol | Molecular formula: C30H50O | | |
|       |            |                  |                | SMILES:C[C@H]1C([C@@]2([C@H]3([C@H]4([C@@]5([C@H]6CC)C)C)C)C)C | |
|       |            |                  |                | | | |
| 14    | Nelumbo nucifera Gaertn | Nuciferine | Antineurotic 0.851 0.009 + + + | Antitussive 0.836 0.003 + + | Antieczematic 0.851 0.010 + + | |
|       |            | Pubchem ID: 10146 | Molecular weight: 295.382 g/mol | Molecular formula: C19H21NO2 | | |
|       |            |                  |                | SMILES:CN1CCC2=CC(=C(C3=C=C2(C(=O)O)OC | |
|       |            |                  |                | | | |
| 15    | Nyctanthes arbor-tristis L. | Nyctanthic acid | Hepatoprotectant 0.897 0.002 + + + | Insulin promoter 0.838 0.004 + + | Antineoplastic 0.826 0.009 + | Chemopreventive 0.814 0.004 |
|       |            | Pubchem ID: 12313631 | Molecular weight: 440.712 g/mol | Molecular formula: C30H48O2 | | |
|       |            |                  |                | SMILES:CC(=C(C3=C=C2(C(=O)O)OC | |

(continued on next page)
| S. no | Plant name | Reported compounds with details | PASS prediction | Pa | Pi | admetSAR prediction |
|-------|------------|---------------------------------|----------------|----|----|-------------------|
|       |            |                                 |                |    |    |                   |
| 16    | Polyalthia longifolia (Sonn.) Thwaites | Liriodenine | Neurotransmitter uptake inhibitor | 0.888 | 0.002 | + + + |
|       |            | Pubchem ID: 10144 | Antineoplastic (colorectal cancer) | 0.688 | 0.005 | + + + + |
|       |            | Molecular weight: 275.263 g/mol | Antineoplastic (colorectal cancer) | 0.786 | 0.014 | + + |
|       |            | Molecular formula: C_{17}H_{9}NO_{3} | Antineoplastic (colorectal cancer) | 0.786 | 0.014 | + + |
|       |            | SMILES: C1OC2@C(O1)C3=C4C(=C2)C=CN=C4C(=O)C5=CC=CC=CC53 | Antineoplastic (colorectal cancer) | 0.786 | 0.014 | + + |
| 17    | Sesamum indicum L. | Sesamin | Membrane integrity agonist | 0.931 | 0.005 | + + + |
|       |            | Pubchem ID: 72307 | Antineoplastic | 0.797 | 0.012 | + + |
|       |            | Molecular weight: 354.358 g/mol | Carminative | 0.761 | 0.004 | + + |
|       |            | Molecular formula: C_{20}H_{18}O_{6} | Carminative | 0.761 | 0.004 | + + |
|       |            | SMILES: C1[O@H]2[C@H](CO[O@@H]2C3@CC4@C(C(C4@C5)OCO6)]CC5=CC=C(C=C5XCO6) | Carminative | 0.761 | 0.004 | + + |
| 18    | Sida acuta Burm.f. | Vasicinone | Antibypoxic | 0.744 | 0.005 | + + + |
|       |            | Pubchem ID: 442935 | Antineoplastic (multiple myeloma) | 0.564 | 0.005 | + + + |
|       |            | Molecular weight: 202.213 g/mol | Antineoplastic (multiple myeloma) | 0.564 | 0.005 | + + + |
|       |            | Molecular formula: C_{11}H_{10}N_{2}O_{2} | Antineoplastic (multiple myeloma) | 0.564 | 0.005 | + + + |
|       |            | SMILES: C1CN2C(NC3@CC=CC=C3C2=O)[C@H] | Antineoplastic (multiple myeloma) | 0.564 | 0.005 | + + + |
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 cytotoxicity 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 glioblastoma (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 glioblastoma (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).

**Table 4 (continued)**

| S. no | Plant name         | Reported compounds with details | PASS prediction | Pa   | Pi   | admetSAR prediction |
|-------|--------------------|-------------------------------|-----------------|------|------|---------------------|
| 19    | Tribulus terrestris L. | Harmine (Pubchem ID: 5280953) M: Molecular weight: 212.252 g/mol | Lysase inhibitor | 0.681 | 0.026 | + + + |
|       |                    | SMILES:CC1=NC=CC2=C1NC3=C2C=CC(=C3)OC | Preneoplastic conditions treatment | 0.628  | 0.019  | + + |
|       |                    | Molecular formula: C_{16}H_{26}N_{2}O | |
| 20    | Vitex negundo L.   | Vitexicarpin (Pubchem ID: 5315263) Molecular weight: 374.345 g/mol | Antimutagenic | 0.928  | 0.002 | + + + |
|       |                    | Molecular formula: C_{19}H_{18}O_{8} SMILES:C1=CC1(C1C(C=O)C1)O | Apoptosis agonist | 0.895  | 0.004 | + + |
|       |                    | Lysase inhibitor | 0.681  | 0.026 | + + + |
|       |                    | Preneoplastic conditions treatment | 0.628  | 0.019 | + + |
|       |                    | Antineoplastic | 0.832  | 0.008 | + |

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