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Traditionally Used Medicinal Plants Belongs to Family Asteraceae for the Treatment of Cancer in Mizoram, Northeast India

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Abstract

The traditional knowledge and use of medicinal plant species from the plant family Asteraceae was reviewed for the treatment of several types of cancers in Aizawl District, Mizoram, Northeast India. Traditional healers and patients suffering from various cancers in the study area were interviewed with the help of local translators to congregate the information for the use of medicinal plants against several prevalent cancers in this part of India. In the present review, we reported 22 plant species which were commonly used for the treatment of various cancers and ulcer. The most common used plant for the treatment of various cancers is *Mikania micrantha* followed by *Ageratum conizoids*. Leaves are the most common part used. The present review outlined the traditional information along with the major phytochemical compounds obtained from the listed plants which may be responsible for their traditional values in the selected study area. We hypothesized that the information could improve the traditional anti-cancer recipes and might contribute to a better national or international health system in future.

Keywords: Anticancer; Asteraceae; Mizoram; Phytochemicals; Traditional Medicinal Plants

Introduction

Plants have always been the important source for the nutrition and therapeutic usage against a notable number of human ailments. Recent phytochemical studies of medicinal plants supported the effectiveness of folkloric medicines. From the ancient time, the plants have been used for curing various diseases and infections. Cancer is the stage of uncontrolled growth of several cells, which can colonize and spread to distant sites of the body. It has many health consequences and can lead to death. In males the most common prevalent types of cancers are lung, prostate, colorectal, stomach, and liver cancers whereas, breast, colorectal, lung, uterine cervix, and stomach cancer are most prevalent in women's. On an average 30% deaths occur due to cancer can be prevented by avoiding key risk factors like tobacco or smoked foods. There is a serious need of the natural cancer control plans to prevent or inhibit the spread of cancer especially in low and middle income countries like India. Recently, World Health Organisation (WHO) has initiated and promoted Cancer Control Programme (CCP) all around the world with a main focus to promote national cancer control policies and ongoing programmes. One important parameter of this programme is to set norms and standards, spread awareness, more importantly encourage evidence based prevention by using traditional information's mainly in remote areas where the medical facilities are limited.

For the treatment of different types of cancers many traditional plants were used by the local practioners. If we look into the phytochemistry of few plants then the discovery of compounds like paclitaxel, vinblastine, vincristine, the camptothecin derivatives are the plant derived agent that made history for the treatment of various cancers. Still many active phytochemical compounds from traditionally used plants are under clinical trial for the promising cancer cure.

Among the plants, family Asteraceae is the largest flowering plant family comprising around 1,600 genera and 30,000 species [1]. The plants are well known to produce foodstuffs, cooking oils, ornamental plants and medicinal plants. Phytochemical studies of number of Asteraceae plants have revealed the presence of various chemical compounds like alkaloids, polyphenols, phenols, flavonoids, terpenes, essential oils etc. Sesquiterpene lactones are the major phytochemicals in the family that have various biological activities. They are supposed to possess antibacterial, antiviral and anticancer potential [2-4].

Mizoram is a small and hilly state possesses rich biodiversity of medicinal plant, with 90.68% forest cover [5]. It lies between 21º 56' N-23º E latitude and 92º 16'-93º 26'N longitude, [6]. Mizo, the local population possesses unique cultures and indigenous practices endemic to this region. Local tribes traditionally use many plants for the treatment of cancer, tuberculosis, diabetes, arthritis skin diseases, allergies etc. There exist traditional practitioners which prescribes herbal preparations in the form of decoctions, teas or to chew orally or the pastes to apply externally.

Cancer in Mizoram: An Overview

Cancer is the uncontrolled growth of cells in the body leading to the death of an individual. Cancer starts with changes in normal cell that include irregulation of cell division and cell death, cell proliferation, invasion, angiogenesis and metastasis. Deformed mass of cells could locate inside the tissue without metastasize or it could invade the other tissues or other part of body. It is a worldwide killer disease that causes more than 7 million deaths per year worldwide. Till date, more than 100 types of cancers have been identified which are classified into different groups such as carcinoma, leukemia, lymphoma and myeloma, and central nerve system by National Cancer Institute (NCI). Major causes for the cancer are the factors, such as dietary habits, smoking, alcohol consumption, infectious viruses, radiation etc [7]. The lifestyle factors seem to be associated for Mizoram having the highest stomach cancers in India [8].

In the recent years, enthusiasm for the use of traditional medicines against many diseases especially for cancer has begun. Discovery of vinca alkaloids, vinblastine, vincristine podophylotoxins like anticancer agents from plants led to the search of novel chemotypes [9]. Plant derived chemotypes are moderate cytotoxic and found to be effective on tumor cells *in vivo* with less side effects comparative to conventional treatment methods [10,11]. According to a European Survey by the use of herbal medicines in the cancer treatment were escalated to 13.9% after the diagnosis of cancer from 5.3% before the diagnosis of cancer [12]. In Mizoram around 89 plants species belonging to 56 families and 68 genera are used as herbal medicines for the cure of various ailments [13]. There are also several reported and few unreported plants which were traditionally used for the treatment of various types of cancers. The present study documented twenty three most commonly used traditional medicinal plants used by the local tribes for the treatment of several kinds of cancers in Mizoram, India. We also listed out the method of preparation and the pharmacological importance of these plants as reported elsewhere. From Mizoram which falls under IndoBurma biodiversity hotspot, this is the first report about the traditional plants belongs to the family Astreaceae having anticancerous potential. The present review will open up the field for the pharmaceutical peoples to understand the chemical composition of the selected plants in future.

Material and Methods

There are many Ethnomedicinal plants used by the local people of Mizoram for the treatment of cancer-suspected diseases and other health problems. Information of the plants used in the treatments of cancer was collected personal with local herbal practitioners and the patients suffering from villages in Aizawl, Mizoram, India (Figure 1). Though they were not very much open about how to prepare the herbal mixture, but gave some glimpses of the name of the plants and for what diseases the plants may be useful. For some traditional medicinal plants like *Anaphalis adnata* and *Leucomeris decora* there is no literature available but still are important traditional medicinal plant. The output plants list consists of local name (mizo) and the common name of the plant. Other information viz. flowering season of the plant, major phytochemicals isolated and the bioactivities were assayed through the literature search. Following are the plants noted from the family Asteraceae used in the herbal preparations for the cancer and other diseases by the Mizo tribal peoples as well.

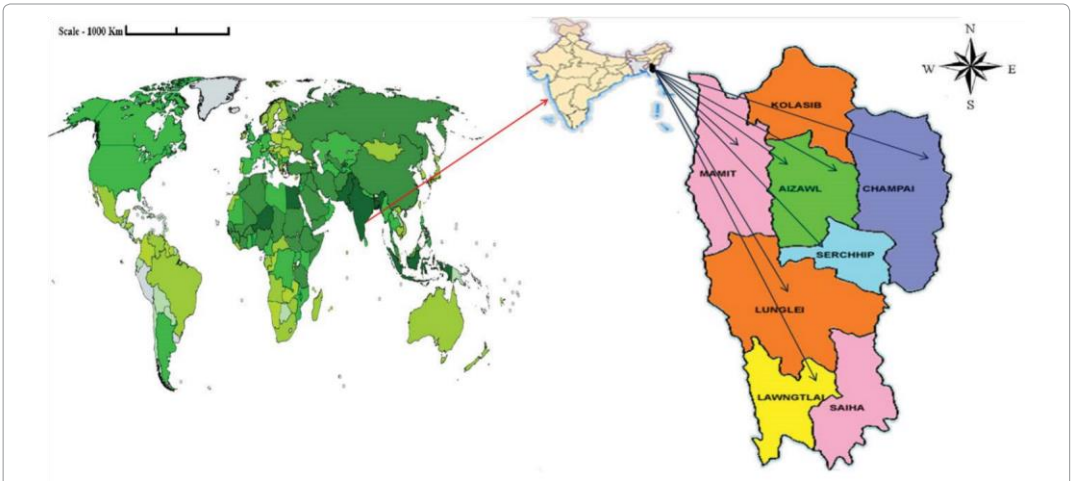

Figure 1: Map showing the sample collection sites from different districts of Mizoram, Northeast India.

Acmella oleracea/ Spilanthus acmella

Local name: An-sa-pui/ An-ka-sa-kir (mizo)

It is also known as toothache plant. The flowering season is during October- December of every year. Major phytochemicals reported from the plant are Spilanthol (*N*-isobutyl amides), [14] saturated and unsaturated alkyl ketones, alkamides, hydrocarbons, acetylenes, lactones, alkaloids, terpenoids, flavonoids, and coumarins. All the plant parts, flowers, leaves, roots, stems and aerial parts are used in herbal medicines. Leaves and stem boiled with water was used for the treatment of stomach trouble and flower head is chewed to have a relief in toothache.

The whole plant paste is used for snake bite. The particular plant is been reported to possess analgesic, antioxidant, anti-inflammatory [15,16], antifungal [17] and anticancer activities [18].

Adenostemma lavenia

Local name: Vai-len-hlo-suak (mizo)

It is also known as sticky daisy and the flowering season in between March-January. Major phytochemicals reported from this plant are Adenostemmoside, Adenostemmoic acid [19]. Traditionally the leaf paste is applied on cuts and wound, insect and caterpillar bites [20], found the *Adenostemma lavenia* plant extract is effective against MK-1 and B16F10 cell lines as well which further proves the potential of existence of anticancerous compounds.

Ageratum conizoids

Local name: Vailenhlo (mizo)

It is also known as goat weed and the flowering season are in February-March or August-September every year. Among the reported phytochemicals from *A. conizoids* are mono and sesquiterpenes, triterpene and sterols, chromene, chromone, benzofuran and coumarin, flavonoids, alkaloids etc. [21]. The plant is traditionally reported to be used for curing various kinds of diseases including tuberculosis, skin diseases, fevers, cuts and wounds. In Mizoram this plant is been used from many years by the local healers for the treatment of stomach cancer. The method of preparation is that the plant roots are cleaned and boiled with the rhizome of *Curcuma longa* and leaves of *Mikania micrantha* in water and the decoction is given orally [22].The plant is also reported by several researchers all around the world to possess antibacterial [23], wound healing, anti-inflammatory, antianalgesic, antipyretic [21] and cytotoxic properties [24].

Anaphalis adnata

Local name: Khaw-te-mei-bu (mizo)

It is commonly known as pearly everlasting and the flowering season for this plant is during May-October. Traditionally the boiled juice of the leaves is applied on cuts and wound to get relieve from infections.

Artemisia vulgaris

Local name: Sai (mizo)

It is also known as Mugwort. The flowering occurs in the plant during January. Few of the reported phytochemicals from *A. vulgaris* are flavones (luteolin, luteolin-7- glucoside), flavonols (kaempferol, quercetin, rutin), coumarins (coumarin, 6,7-dimethoxy-coumarin) [25]. The plant is traditionally used to cure a wide range of ailments including malaria, bacterial infections, inflammation, menopausal and menstrual disorders. Traditionally decoction of the roots or leaves is given orally in fever, stomach-ache, asthma etc. The plant has showed significant cytotoxicity against HL-60 leukemic [26], HEPG2 [27], Human prostate cancer PC-3, Human breast carcinoma T47D and colon cancer RKO [28] cancer cell lines cells.

Bidens pilosa

Local name: Vawk-pui-thal (Mizo)

It is also known as Black-jack and the flowering season in during February to April every year. The plant is very well studied and many major phytochemicals are reported like terpenoids, phenylpropanoids, aromatics, porphyrins, flavonoids, [29]. *B. pilosa* is been reported for the treatment of various diseases such as inflammation, immunological disorders, digestive disorders, infectious diseases, cancers, metabolic syndrome, wounds, and many others [30]. Generally whole plant is been used in herbal medicinal. Among the specific parts, aerial parts like leaves, shoot and stem are also been used as an ingredient in teas or herbal medicines in several countries. Its shoots and leaves (dried or fresh) are utilized in sauces and teas. Sundarajan et al., 2006 and kumari et al., 2009 determined the anticancer activity of *B. pilosa* extract against HeLa, KB, HepG2, CaCO2 and MCF7 cancer cell lines [31,32].

Blumea lanceolaria

Local name: Buar-ze (mizo)

It is commonly known as lanceleaf blumea ans gives flowers during February-April. The plant is well studied for its phytochemical constituents and few major compounds reported are methyl thymol, p-Cymene, and l-hexadecanol [33]. The local tribes of Mizoram used juice of *Blumea* leaves to treat stomach ulcer, asthama, tuberculosis, skin diseases, sores, scabies etc. Rosangkima and Prasad 2004 determined the antitumor activity of *B. lanceolara* leaves against murine ascites Dalton's lymphoma in mice [34].

Chromolaena odorata/Eupatorium odoratum

Local name: Tlang-sam (mizo)

It is also known with the name of Christmas bush and give flowers during December- January. Some of the important phytochemicals reported from this palnts are 5-hydroxy-7,40– dimethoxyflavanone, 20-hydroxy-4,40,50,60–tetramethoxychalcone, and 1,6-dimethyl-4(1-methylethyl)naphthalene (cadalene) [35]. Traditionally, the leaf juice is applied on fresh cuts and wound to fight against infections and it is been reported to have several activities like antibacterial [36,37], anticancer [35,37,38], antifungal [39], anti-inflammatory [40,41] and anti-malarial [42,43]. The plant could be an interesting candidate for the discovery of the novel bioactive therapeutically active agents.

Chrysanthemum indicum

Local name: October-par (mizo)

It is also known as chrysanthemum, the plant flowers during October till March. The plant is not well studied for the presence of phytochemicals, only few reported compounds are from sesquiterpenes. Traditionally the flowers are used to make tea for digestive purpose. In several other countries the *C. indicum* is used for the treatment of colitis, stomatitis, cancer, fever, sores, vertigo, inflammation and hypertension. Plant is also been reported to possess anti-inflammatory [44], hepatoprotective [45], antimicrobial [46-48] and anticancer properties [49].

Cirsium shansiense

Local name: Len- hling (mizo)

It is also known as Canadian thistle which mainly flowered during October every year. Few of the reported phytochemicals from this plant are ciryneol C, scopoletin, pectolinarigenin7-O-glucopyranoside, acacetin and 6,7-dimethoxycoumarin [50]. Traditionally the plant is been used for the treatment of different ulcers

and also used as diuretic, haemostatic and anti-inflammatory. The plant also has antimicrobial [50,51] and anticancer [52] potential.

Crassocephalum crepidioides

Local name: buar-thau (mizo)

It is also known as Thickhead and the flowering season for this plant are in May to December. Few of the broad phytochemicals reported from this plant are tannins, flavonoids, steroids, coumarins [53]. Traditional medicinal uses of the plants are that the leaf juice is taken for indigestion and stomachache. Leaf paste is applied to heal cut and wounds to fight against microbial infections. Different plant parts are also been used in the herbal preparations for the treatment of fever, hepatitis and inflammations. The plant is reported to possess hepatoprotective [54], antitumor [55,56], and antibacterial [57] activities.

Cyanthillium cinereum

Local name: Buar (mizo)

It is also known as purple fleabane and gives flowers mainly during February. Traditionally plant decoction is used to treat urinary tract infections and fevers. *Cyanthillium cinereum* has therapeutic potentials against dysentery, diarrhea, cough, cholera, impotency colic pain night-blindness [58] asthma [59] and cancer [60].

Dichrocephalum integrifolia

Local name: Vawk-ek-a-tum-tual (mizo)

The plant flowers during May-June. Some of the reported phytochemicals from this plant are stearic acid, stigmasta-7, 22-dien-3-ol, alpha-amyrin, epifriedelanol, methyl stearate and tritetracontane [61], eudesmane [62]. Traditionally the plant is been reported having antimicrobial [63,64] as well as anticancer [64] potential. Plant is traditionally used for wound healing, to treat mouth and stomach ulcers and microbial infections.

Galinsoga parviflora

Local name: sazu(pui)chaw (Mizo)

It is also known as quick weed and the flowering season is during June to September every year. Some of the reported phytochemicals obtained from *G. parviflora* are galinsosides A and B [65]. Traditionally the leaves and stem of the plant are been used in the herbal preparation for fever, diarrhea, cuts and wound. *G. parviflora* is also reported to have hepatoprotective, hypoglycemic, antioxidant, cytotoxic, and antimicrobial activities [66].

Helianthus annuus

Local name: Ni-hawi (mizo)

It is commonly known as sunflower and the flowering season is in August to September. Major phytochemicals reported are Heliespirone [67], Heliannuol E [68], Helikauranoside A [69]. Medicinally the plant is used as food and medicine all around the world and most importantly the seeds are been used for the production of cooking and essential oil. Leaves, stem, flower and seed oil all possess active principle and plant has potent antioxidant and also possess antimicrobial [70,71], anti-inflammatory [72] and anticancer potential [73,74]. Traditionally the leaf paste is applied to wounds, swellings, and insect bites. Flowers are taken as tea for the treatment of malaria and lung diseases.

Inula cappa

Local name: Hmei-thai-sa-tul (mizo)

It is also known as sheep's ear and flowers during September and October. Sesquiterpens lactones [75,76], and phenolic glycosides [77] are reported as major phytochemicals from this plant. Traditionally the leaf juice of *Inula cappa* is been used locally for the treatment of jaundice. Decoction of the root is also been used to treat peptic ulcer, indigestion and fever.

Leucomeris decora

Local name: Tlangham (mizo)

The plant flowers during February to March every year. It is an Asteraceae shrub and been used traditionally for curing many ailments especially the leaves and stem. The plant becomes locally rare due to rapid habitat destruction and fragmentation, together with unrestricted collection for medicinal use. Thus it has been listed in the IUCN red list of threatened species [78].

Mikania micrantha

Local name: Japan-hlo(mizo)

It is also known as bitter vine and flowers during December till January each year. Mikanolide: a sequiterpene dilactone [79], is the major phytochemical reported from this plant. It is a perennial vine of which leaves are used to treat fever, diarrhea, dysentery, insect bites, scorpion sting and cuts by traditional peoples. Several reports are available for its anticancer and antitumor activities [80-82].

Senecio scandens

Local name: Sai-ekk-hlo(mizo)

The plant flowers in February and March. Several phytochemicals like pyrrolizidine alkaloids and sesquiterpenes [83], jacaranone [84,85], phenolic acids [86] were reported from *S. scandens*. In Mizoram local practitioners are using this plant for the treatment of stomach cancer and other different type of cancers. Juices of the leaves are applied to chronic ulcers. Pyrrolizidine alkaloids recovered from this plant are proven to be hepatotoxins and carcinogens [87]. Plant has shown potent antimicrobial [88,89], anti-inflammatory [90], antitumor [91] and anticancer activity [92] as well.

Siegesbeckia orientalis

Local name: Ansa-pui-suak(mizo)

It is commonly known as st. paul's wort, flowers during October-November every year. Several phytochemicals like sesquiterpene lactone: orientin [93], diterpenoids: Kirenol and ent-16β,17-Dihydroxy-Kauran-19-Oic Acid (DHKA) [94]. *S. orientalis* is been reported for anti-inlammatory [95,96], anti-proliferative [97] and anticancer activity [98]. Leaves paste is applied against snakebites and insect bites. Decoction of the aerial part is given to treat allergies, skin diseases, rheumatic arthritis and inflammatory diseases.

Sonchus arvensis

Local name: Khuang-lawi (mizo)

It is also known as corn sow thistle which give flowers during September till December. Few of the phytochemicals reported from this plant are sesquiterpene lactones [99], flavonoids [100] and terpenes [101]. The plant has been used in folk medicine for the treatment of jaundice, cough, bronchitis, chronic fevers and inflammation. It has been reported to possess anti-inflammatory and antipyretic effect in rats [102] along with antioxidant and cytotoxic [103] activities.

Tithonia diversifolia

Local name: Bawng-pu-pang- par (mizo)

It is also known as Mexican sunflower and the flowering season is during NovemberDecember. Tagitinins, tirotundin, flavones [105] were reported as major phytochemicals from *T. diversifolia*. The plant is generally grown for ornamental purpose but possess medicinal properties as well. Traditionally the plant is been used for the treatment of diabetes mellitus, stomach pains, indigestion, sore throat and liver pains [103]. Flower head is used by local healers for the treatment of wounds and bruises. Plant seems to have an anti-inflammatory [104] anti-diarrhoeal [105], anti-amoebic and spasmolytic activities [106,107].

Conclusion

We documented twenty two traditionally used medicinal plants used by the local tribes

of Mizoram, Northeast, and India for the treatment of several types of cancers and other human ailments. The paper also describes the important information like their local name, flowering season and major phytochemical compounds investigated from these plants elsewhere. As due to over utilization and population explosion, these plants which were used in local health traditions are gradually becoming extinct. The present review will alert the environmentalists and researchers to take steps to preserve or conduct modern scientific studies of these traditionally important plants. These types of studies not only

can lead to probable discoveries of new bioactive pharmacologically useful compounds, but also such discoveries can be an encouragement for the preservation of the forest region. We conclude that domestication of these traditionally important wild medicinal plants should be of utmost importance for the sustainable development.

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