



Significance of documentation of traditional knowledge of herbal medicinal practitioners for the herbal drug discoveries-A comprehensive review

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Abstract

In many countries, traditional medicine is the first line of defense when it comes to treating illnesses. Indigenous peoples still carry and orally transmit a considerable deal of traditional knowledge regarding the usage of medicinal plant species. Ethnobotanical studies have great importance in enhancing our knowledge about the plants used by the tribal communities; contribute to conserving plant biodiversity and traditional knowledge. Modern medicinal know-how documentation may lead to the discovery of novel medications and help to conserve, manage and utilize plant resources in a sustainable manner. Current research status on ancient traditions and modern advancements about medicines used by the traditional folk healers are of great socio-economic significance to the world of medical science by identifying potential medicinal plants and revealing the therapeutic drug molecule to the modern civilization. This paper describes research done on traditional knowledge, family secrets of medical practitioners, and their approach to curing various ailments including the threats to herbal biodiversity in the rural and forest area. The ethnobotanical or medicinal survey approach should also emphasize on documentation of threats to the herbal biodiversity and provide suitable restoration approaches that prevent the extinction of certain valuable medicinal Plant species. Despite, phytochemical analysis, identification of key bioactive molecules, as well as investigation of their therapeutic potential for various diseases, are need of the hour for developing strategies for novel herbal drug molecules.

Keywords: traditional knowledge, medicinal practitioners, herbal remedies, alternative medicine, phytochemicals, therapeutic potential

Introduction

Survey and documentation on traditional knowledge of medicinally important plants, their uses, and therapy approaches are essential to lay a foundation for herbal discovery research. Many researchers and practitioners have worked on ethnobotany in various aspects. Historical evidence proved that ancient people like Aryans (4000BC), Sumerians (3,500BC), Chinese (3000BC), and Egyptians (2500 BC) knew about the medicinal plants and recorded them in texts and manuscripts [1].

Since 1960 Jain S.K. from BSI started intensive field study among the tribes of central India and he derived the methodology of Ethnobotany, so he is affectionately known as "Father of Ethnobotany" [2,3].

In the ethnobotanical study, the threat to the herbal biodiversity is also to be documented, addressed, vital recovery measures or recommendations also to be provided for their restoration. Local hill farming methods such as "slash and burn" and encroaching civilization is causing the local uses of the plants to dwindle, thus it's important to document the native applications of these weeds now before the information is lost [4].

Overutilization of forest-based products is to be restricted for the local community. The ethnobotanical investigations of 146 plants used for medicines, veterinary medications, food, fodder, household items, building materials, and other social and religious ceremonies among the tribes of Ranchi, Gumla, Lohardaga, and Palaman districts of Bihar [5].

Among the herbs, the Orchids are an important group of plants in India's traditional medical system and used since the time of the Rig Vedas, but their medicinal importance has been subdued in front of their wide population as ornamental. Many orchids play a major role as alternative medicine as they have abundant in alkaloids, flavonoids, glycosides, carbohydrates, and phytochemicals [6].

Momordica L includes *M. charantia* var. *muricata*, *M. charantia* var. *charantia*, *M. dioica*, and *M. sahyadrica* were found in the Western Ghats, one of the mega diversity hotspots. Traditional uses of these species include food, medicine, and cosmetics. Taboos and religious beliefs relating to their domestication and folk taxonomy were reported [7].

Uncontrolled forest resource exploitation to meet demand had resulted in the extinction of many species. Many tribes in Molakalmuru taluk of Karnataka, India have special knowledge of plants, and documentation on the preparation of drugs to cure various diseases by the tribe and medicinal practitioners were reported [8]. Western Ghats' hilly regions in Karnataka have sponsored several thousand medicinal plants along with other rich flora and fauna and have also helped to establish traditional medicine knowledge and folklore to cure various diseases and ailments. 100 plants information was documented by local people, vaidyas, and physicians to cure various health-related problems [9]. Forests in the Chitradurga area of Karnataka, India, were designed to promote a great floral diversity and 366 herbs

have been recorded concerning their significance in Indian medicine. Forests are a wealth of food and medicine for forest dwellers and those living in and around forests. This often has a direct impact on nearby people's lifestyles^[10].

Herbal healers are usually interviewed by the researchers and their traditional knowledge have been documented around the world and in Western Anatolia, Turkey, in 17 distinct locations of the Afyonkarahisar region, 48 traditional herbal healers were polled to develop an inventory of herbal treatments often used in the treatment of diabetes and they discovered a revolutionary technique to treat diabetes^[11].

In southern mainland Yemen, traditional knowledge of medicinal plants is being passed down orally from generation to generation^[12]. The knowledge gathered about traditional medicinal plants will serve as a useful resource for developing herbal drug industries and improving the region's economy^[13].

Phytochemical extraction and analysis

Plants used in Ayurveda can offer increased activity and reduced toxicity to biologically active molecules and provide lead structures to produce modified derivatives. Ethnobotany and ethnomedicinal studies are recognized as the most viable methods to classify new medicinal plants or to re-focus on those previously identified for bioactive constituents. The ongoing search for natural plant products to use as medicinal products has served as an opportunity for exploring methodologies involved in obtaining the appropriate plant materials and thus testing their components. The aerial portions of *S. pubescens* yielded a novel steroidal alkaloid, solanopubamine, according to ¹³C NMR, ¹H NMR, IR, mass analysis, and chemical degradation procedures^[14]. The leaves of *S. pubescens* Willd were used to isolate certain methyl ethers of quercetin and kaempferol. All of the methyl ethers were discovered to be 3-methyl ethers with a free 5-hydroxyl ring and this is the first time that methyl ethers have been reported from the Solanaceae family^[15]. Therefore, it is of taxonomic significance, representing the possibility of the further presence of 3-O-methyl ethers, besides, the isolation of kaempferol's 3-O-glucoside and 3-O-runnoside is in support of the earlier reports on the abundance of glycosides in the Solanaceae. Similarly, spectral and chemical approaches were elucidated. Two new steroidal alkaloids from the *S. pubescens*, solanopubamides A and B from aerial parts, were isolated. Spectral and chemical approaches were used to elucidate their structures^[16].

Botanicals were commonly employed in their raw form in the earliest generation of plant medications. Following the industrial revolution, the second generation of plant-based medications emerged to fill the gap to separate "their active constituents" supported the scientific processing of plant extracts. The second generation of phytopharmaceutical substances were pure molecules and a few of them were significantly more pharmacologically active than their synthetic counterparts. A top-bottom strategy is usually followed within the production of "third-generation" phytotherapeutic agents. It consists of performing a primary clinical review of the treatment modalities and therapy as practiced by conventional physicians or by folk medicine practitioners. Several pharmaceutical companies work to develop natural product drugs by isolating the so-called active molecules from plant extracts^[17].

Carbohydrates, saponins, oils & fats, alkaloids, and flavonoids were found in various extracts after the preliminary phytochemical screening of *S. pubescens* dried fruit material. Interestingly, the ethanol extract contains alkaloids only. This study assisted us in identifying cytotoxic chemicals that are thought to be significant in the exercise of anti-tumor capabilities^[18].

The studies on antidiarrheal operation on a model of diarrhea caused by castor oil in rats using methanolic leaf extract of *S. pubescens* and the major findings showed substantial antidiarrheal activity^[19]. Although these neuropharmacological effects may be attributed to flavonoid involvement, the *S. pubescens* leaf displayed substantial anticonvulsant and sedative effects, providing evidence for its folklore use. Alkaloids, resins, glycosides, sugars, sugar reduction, fats, and oils, flavonoids, and terpenoids have all been found in phytochemical exploration^[20].

Different extracts contain oils and lipids, alkaloids, flavonoids, carbohydrates, saponins, coumarins, and phenolics, according to the early phytochemical screening of the fruit and stem bark. Surprisingly, the ethanol extract solely contains alkaloids. The quantitative analysis revealed that *S. pubescens* has a high concentration of phenolics, followed by flavonoids, alkaloids, saponins, carbohydrates, and oils, providing a strong case for selecting this plant for testing possible pharmacological qualities^[21].

The investigation on the acute toxicity, antioxidant activity *in vitro*, and anti-inflammatory activity *in vivo* of hexane and chloroform extracts of *S. pubescens* fruits and stem cured inflammation in rats caused by carrageenan and cotton pellets. Their study revealed that the *S. pubescens* fruit essential oil, fruit chloroform extract, stem hexane extract and stem chloroform extract demonstrated substantial 2, 2-diphenyl-1-picrylhydrazyl, hydroxyl radicals, superoxide anion radicals, nitric oxide radicals, 2, 4, 6-tripyridyl-s-triazine radical scavenging effect, inhibition of lipid peroxidation, total declining power, and total antioxidant activity. The present report has valuable and supporting data relevant to the use of ethnomedicine also considering the herb *S. pubescens* as a reservoir of novel anti-inflammatory agents^[22].

Studies on phyto therapeutic compounds using HPLC analysis

The pharmacological activities of alkaloids as phytoconstituents are well established. Alkaloids can be found in the roots, stems, leaves, flowers, fruits, and seeds of plants. Solasodine is a nitrogen-binding aglycone member of the glycol alkaloid family. The Solanaceae family consists of a range of plants with a variety of medicinally important natural products, mainly steroidal lactones, glycosides, alkaloids, and flavonoids^[23]. High-pressure liquid chromatography with low-wavelength UV detection was used to separate and analyze solasodine-related chemicals (solasodine, solasonine, solamargine, and solasodine)^[24].

All known methods for separating Solanum steroid alkaloids offer the best separation of saturated and analogs, while HPLC delivers the best separation of saturated and analogs^[25]. The chromatographic conditions can differ according to the alkaloid mixture composition. Based on preliminary findings, a solvent mixture of acetonitrile-methanol (85:15) was used to separate partially characterized dihydroxy steroidal alkaloids at a flow rate of 0.5 ml min⁻¹ which

provides better resolution. If there are substances in the polarity order or less polar than solasodine in the alkaloid mixture, the solvent mixture of 60:40 at a flow rate of 1 ml min⁻¹ would result in shorter analytical time without substantial loss in resolution. Environmental factors affecting solasodine content, chemical and physical agents that increase it, and aglycone extraction and purification procedures in *Solanum* species are well described [26].

Using a base-deactivated C-8 column and an acidic mobile step, an improved isocratic high-performance liquid chromatography method for assessing solasodine was created for use in steroid drug commercial development [25]. Sharp symmetrical peaks were found and a linear relationship between the volume of injected solasodine and the region below the peak was detected. The approach detects and quantifies solasodine in plant tissue samples at levels as low as 0.40 mg, and it records the amount of solasodine in the sample rather than the "solasodine equivalents" calculated by previous methods.

The quantification of solasodine was achieved by an independent comparison of the present peak area of both samples with the regular sample at a known concentration. Nuclear magnetic resonance (NMR), mass, and Infrared (IR) spectroscopy have confirmed the structure of diosgenin and solasodine and the lowest detectable limit of diosgenin and solasodine was found up to 20 ng and 10 ng respectively with good resolution and separation of diosgenin and solasodine from other *S. xanthocarpum* constituents in a single HPTLC method. The method is quick, simple, and accurate for quantitative monitoring of the dried fruits and extracts of diosgenin and solasodine in *S. xanthocarpum* [27]. Solasodine is an alkaloidal steroid based on a skeleton of cholestane C27. Several analytical methods have provided separation and quantitative determination as well as highlight Solasodine's pharmacological activity, as well as its analytical and tissue culture techniques, which may aid researchers in developing novel compounds for the treatment of various illnesses [28]. Investigations on the establishment of biomass to produce solasodine under *in vitro* conditions; its quantification and validation with good linearity, precision, accuracy, and robustness are recorded in *S. xanthocarpum* plant for the first time using reverse-phase high-performance liquid chromatography (RP-HPLC) process [29]. To isolate and evaluate the steroidal glycoalkaloids (SGAs) and the steroidal glycoalkaloid aglycones (SGAAs) solasodine, a precise and high-performance liquid chromatography (HPLC) method was reported [30]. The current research contests to indicate the correct mobile phases combined with the use of fast and efficient chromatographic liquid column to establish a simple HPLC gradient elution method which was successful in separating both SGAs and SGAAs of interest in *solanum* extract. Successfully obtained the optimization separation conditions for all alkaloid material at low pH of 3.14 at 50°C in less than 7.0 minutes. The best separation parameters such as the limit of detection (LOD) of 0.5 µg/ ml, limit of quantitation (LOQ) of 0.7 µg/ ml and linear dynamic range was obtained using strong liquid column C-18 (50 x 4.6 mm I. D) of 3 µm particle size.

Studies on plant phytochemicals and their anticancer activity

The second leading cause of death in the world is cancer. Conventional cancer treatments cause severe side effects

and at best, only increase the lifetime of the patient by a couple of years. Thus, cancer management can benefit from the potential of alternative therapies. The desire for using alternative methods or approaches to cancer care is on the upsurge. Natural products were traditionally the most important source of medicines and product leads. Anticancer chemicals are either natural products or derived from natural products, which explains their dominance in cancer chemotherapeutics. Plants are utilized to treat ailments all around the world, and plant secondary metabolites research continues to provide new medications. Natural products with a leading role in chemotherapy for cancer account for approximately 74%. The world's biodiversity offers a tool of limitless structural diversity primarily on anticancer compounds for bioprospecting through international drug discovery programs.

The importance of plant-derived chemicals in reducing the incidence of colon cancer and preventing tumor growth and spread in trial animals has been highlighted in epidemiological and experimental investigations [31]. About 25 percent of the drugs used in the last 20 years are derived directly from plants while the remaining 25 percent are chemically modified natural products. Nonetheless, for bioactive compounds, only 5-15% of the approximately 250,000 higher plants have ever been studied. Solanolactosides A, B (1, 2), and two additional glycosides of spirostanol, namely torvosides M, N (3, 4) are the novel C-22 steroidal lactone saponins isolated from ethanol extract from the *S. torvum* aerial segments. The cytotoxicity of the saponins (1-4) against a group of human cancer cell lines was assessed *in vitro*, compounds 3 and 4 display important cytotoxic activity [32].

MTT assays were used to assess the antiproliferative activity of ethyl acetate extract of *S. anguivi* against human liver carcinoma cell line (HEpG-2) and breast cancer cell line (MCF-7) cell lines. Using the methyl thiazolyl diphenyl-tetrazolium bromide (MTT) assay, the anti-proliferative activity of the ethyl acetate extract of *Solanum anguivi* against HEpG-2 and MCF-7 cell lines was investigated at various doses, and cell viability was reduced by up to 50%. The exploration showed that ethyl acetate extract of *S. anguivi* has anti-cancer properties [33]. Aqueous extracts of *S. nigrum* leaves have an important ingredient for the diagnosis of cancer in many conventional Chinese medicines but there is a lack of evidence to validate its efficacy in colorectal cancer suppression. The efficacy of tumor suppression against human colorectal carcinoma cells was tested and found to have cytotoxicity in tumor cells for the development of alternative colorectal cancer chemotherapy [34].

S. pubescens has been used for the prevention of cancer in traditional and folk medicine. The effect of methanol extract of leaves on Dalton's ascitic lymphoma (DAL) in Swiss albino mice of the intraperitoneally injected cell line and found that all the values of cancer monitoring category were found to be statistically significant [35].

In MCF-7 cells, the anticancer activity of methyl caffeate derived from *S. torvum* fruit and the molecular mechanisms of action were investigated, and ethyl acetate extract was found to have substantial cytotoxic activity [36]. Hydro ethanol extracts of the *S. torvum* leaves were tested against the human fetal fibroblast cell line (MRC-5) and revealed the extract had the highest cytotoxicity (CC₅₀) rating and the best selectivity index (SI) 31.25 index [37].

The crude extract of ripened fruits of *S. aculeastrum* as well as the aqueous alkaloid-enriched fraction, exhibited remarkable cytotoxicity and P-glycoprotein (P-gp) inhibition towards both cancerous and non-cancerous cell lines viz colon carcinoma (Caco-2), breast adenocarcinoma cell lines (MDA-MB-231), breast carcinoma (SK-Br3), prostate carcinoma (DU145), hepatocarcinoma (HepG2), breast carcinoma (MCF-7), preadipocytes (3 T3-L1), mouse fibroblast cell lines (SC-1) and myoblast (C2C12) cell lines. Solamargine has been identified as responsible for potent, non-selective cytotoxicity and inhibition of P-gp and the aqueous fraction of solamargin enriched with alkaloids improved the cytotoxicity of doxorubicin by additive activity in select cell lines, while in others it had indifferent and antagonistic reactions^[38].

Three naturally occurring glycoalkaloids (solasonin, solasodine, and solamargine) isolated from the methanolic extract of *Solanum melongena* fruit peels showed antiproliferative activity against two different susceptible lines of liver cancer cells (Huh7 and HepG2)^[39].

Plant phytochemicals and antimicrobial activity exploration

The use of plant extracts in herbal medicine dates to ancient times around the world is still the basis of many drugs in modern medicine. A significant number of plants in the conventional method are believed to contain antibiotic properties, which are also commonly used by indigenous communities around the world. Plants are a source of substantial quantities of drugs for multiple groups, including antispasmodics, emetics, anti-cancer, antimicrobials, etc. Phytomedicines derived from plants have shown considerable promise in treating even the most difficult infectious disorders, such as opportunistic AIDS infections. Plants containing protoberberine and related alkaloids, picralima-type indole alkaloids, and Garcinia biflavonones have been employed in traditional African medical systems to combat a wide range of microorganisms^[40].

Ethyl acetate (EtOAc) extracts of fruit from *S. torvum* fruits were found to have antimicrobial activity against certain bacterial species. MIC and MBC values ranged from 2.5 mg/ml to 20 mg/ml, with MBC values ranging from 5 mg/ml to > 20 mg/ml. The bacteria *P. aeruginosa* was the most responsive to the EtOAc extract's impact and the most immune bacteria was *S. epidermidis* developed an inhibition zone of 7.40 mm ± 0.53 mm compared with gentamicin of 20.7 mm ± 0.21 mm^[41]. Methanol leaf extracts of *Acacia nilotica* and *Sida cordifolia* exhibited the strongest antibacterial activity against *B. subtilis* while *Ziziphus mauritiana* leaf extract confirmed major action against *Xanthomonas axonopodis* and leaf extract of *S. cordifolia* demonstrated substantial activity against all bacteria studied. Bark and leaf extracts of *A. nilotica* demonstrated strong antifungal action against *Aspergillus flavus*, *Ziziphus mauritiana* and *Tinospora cordifolia*^[42]. Antimicrobial activity studies showed significant amounts of antibacterial activity on the four bacteria examined but there was no antifungal activity among the examined fungi while the extracts showed the presence of alkaloids, flavonoids, and other fatty acids, such as palmitic and oleic acids in the GC-MS analysis^[43]. Methanol and aqueous extracts of the leaves of five medicinal plants, *Solanum nigrum*, *Solanum surattense*, *Solanum torvum*, *Solanum trilobatum* and *Solanum melongena*, have demonstrated significant action

against *Xanthomonas campestris* and *Aeromonas hydrophila*^[44]. *S. torvum* methanolic fruit extract spectroscopic data elucidated the presence of methyl caffeate and methyl caffeate's antibacterial activity (zone of inhibition) ranges from 0 to 22 mm. *P. vulgaris* had the lowest minimum inhibitory concentration (MIC) of methyl caffeate, followed by *K. pneumonia* and *M. tuberculosis*. Methyl caffeate was validated as a strong antimicrobial activity and powerful anti-mycobacterial^[45].

Using the agar well diffusion method, the antibacterial properties of chloroform, ethyl acetate, and methanol leaf extracts of *S. anguivi*, *S. pubescens*, *S. surratense*, *S. nigrum*, *S. torvum*, and *S. trilobatum* against human infections were investigated: *Micrococcus luteus*, *Klebsiella pneumoniae*, *Vibrio cholera*, *Staphylococcus aureus*, *Candida albicans*, *Candida tropicalis* and *Candida parapsilosis*^[46]. *S. aureus*, *M. luteus*, *V. cholera*, and *K. pneumoniae* were all effective against four human infections, as well as three fungal species, *Candida albicans*, *C. parapsilosis*, and *C. tropicalis*. *S. anguivi* leaf extract displayed the best antimicrobial activity. Plants can be used for drug discovery studies as well as clinical use against pathogens like *Bacillus subtilis*, *Escherichia coli*, and *Aspergillus Niger*^[47].

The ethyl acetate fruit extract of *S. pubescens* inhibited the growth of *Bacillus subtilis* and *Xanthomonas sp* in the *in-vitro* studies whereas ethanolic fruit extract has been restricted to inhibit *Bacillus subtilis*. Furthermore, stem bark extracts showed potential inhibition of *Bacillus subtilis* and *Escherichia coli*^[48]. The antimicrobial activity of dried fruits ethanolic extracts of *S. torvum* proved antimicrobial activity against most microbes tested^[49]. While the bactericidal activities of *S. torvum* extracts were greater in Gram-positive than in Gram-negative bacteria^[50]. The investigation on the antibacterial effect of *S. xanthocarpum* showed the maximum activity trailed by the *S. torvum* and *S. nigrum*^[51]. *In-vitro* antimicrobial activity of methanolic extracts of *S. nigrum*, *S. surratense*, *S. sysimbrifolium*, *S. villosum*, *S. torvum*, *S. diphyllum*, and *S. incanum* was tested against two gram-positive (*Bacillus subtilis* and *Staphylococcus aureus*) and three gram-negative bacteria (*E. coli*, *Salmonella typhi* and *Proteus vulgaris*) and the zone of inhibition results revealed that methanolic extract of *S. sysimbrifolium* was effective to all the bacterium, while *S. aureus* was most susceptible to all extracts^[52]. The antimicrobial properties of *S. incanum* fruit, root and stem extracts in ethanol and aqueous extracts were tested against two gram-negative bacteria (*Escherichia coli* and *Salmonella typhi*) and two gram-positive bacteria (*Bacillus subtilis* and *Staphylococcus aureus*), with the ethanol leaf and fruit extracts showing the greatest growth inhibition in *B. subtilis* and *S. typhi*, respectively^[53].

Conclusion

Ethnobotanical and medicinal survey, documentation and updating data base of traditional knowledge reveal many useful information for developing novel herbal drug molecule for the present health crisis, various existing and emerging diseases as well. This research must include the biodiversity status of various herbs used by the medical practitioners and the locals to update the threats if any due to climate change or over exploitation or habitat destruction and to develop suitable restoration strategies to avert the precious herbal species loss and extinction.

Conflict of interest

The authors declare no conflicts of interest.

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