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An Ethnobotanical Study of Medicinal Plants Traditionally Used for Treatment of Hair Problems in Nuapadhi Village from Baleswar District of Odisha, India

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Abstract: Ethnobotanical study encompasses the traditional use, management and conservation of plants and plant products with medicinal significance. For centuries people of indigenous habitat have developed their own unique knowledge of local plant and their optimum utilization for human benefit, however most of this knowledge is not well documented and passed on by word of mouth. The present study, was undertaken to ascertain and document the indigenous knowledge of local rural people of Nuapadhi village from Baleswar district of Odisha that enable them to identify plants with medicinal properties, formulate and administer the curative mixture to treat various ailments with special focus on hair related problems. Total 100 informants (65 females and 35 were males) were interviewed to collect information on medicinal plants usage for treating hair problems. Data was collected on the basis of semi-structured interview, field visit and group discussion and analyzed using statistical tools. The study was conducted from November 2021 to May 2022. A total 24 botanical families including 34 different plant species was surveyed to be used to treat various hair related problems. Asteraceae and Rutaceae was observed to be most dominant. Herb was identified as the dominant medicinal plant habit followed by tree and shrub. Leaves are used mostly for preparation of extracts to administer for treating hair diseases. Interestingly the informants in the current study area showed positive correlation between educational qualification and knowledge regarding medicinal plants. The study area of Nuapadhi village is rich in medicinal plants diversity. In order to protect and conserve traditional knowledge participation from both local and government agencies is a necessity of the present time.

Keywords: Medicinal plants, Pharmacognosy, Ethnobotany, Odisha, Traditional knowledge

INTRODUCTION

Studies on rural population are important to understand and maintain the traditional knowledge passed on between generations and discover new species for pharmaceutical production. Ethnobotanical studies have been undertaken by humans since time immortal. Plants have been an integral part of human civilization. Apart from fulfilling basic needs like food and shelter, man has used plants to sought cure for various diseases[1]. Documentation of medicinal use of plants through ethnobotanical studies facilitates not only development of present-day drugs but also for plant conservation[2]. Traditional medicines have been in use for over thousand years and provide primary health care at the community level especially in the rural areas[3].

Ethnobotanical studies revolving around use of plants for healing purpose which are popular in their respective societies are being carried out all over the world[4]. Around 60-85% of populations in developing countries rely on traditional medicines. Employment of traditional medicines for healing purpose of different ailments is widely practiced in Himalayan mountains[7], India[8], South-Eastern Bangladesh[9], Indonesia[10], Kenya[11], Ethiopia[12] and Egypt[13] to name a few. Traditional knowledge on utilization of plants is usually passed on orally and is available with certain community leaders and is often not documented. Such orally preserved indigenous knowledge is prone to loss if left undocumented for future use[14-17]. Conservation and dissemination of such data support to create a knowledge pool between different communities of the world. Thus, documentation of such useful knowledge is absolutely necessary and is accomplished by ethnobotanical research[18]. Such studies not only add to the current knowledge but also offer a foundation for future analysis about the pharmacognosy of the native plants[19].

Odisha lies between 17^0 48”-22^0-94”N latitude and $81^0$24”-$87^0$29”S Longitude[20]. Odisha rich in biodiversity. The ethnobotanical investigation in this area has led to systematic compilation of various indigenous plants used by tribals for their multifaceted needs. The objective of the present work is (i) to document the traditional plant species used by the rural people of Nuapadhi village of Baleswar district, Odisha for treatment of hair problems, (ii) validate the degree of fidelity and concurrence among local inhabitants & (iii) establish the correlation between the number of medicinal plant species known and the levels of education and age.

MATERIALS & METHODS

Study Area: the study was conducted in the rural Nuapadhi village which belongs under Remuna tehsil of Baleswar district, Odisha, India. It is situated 21`00º N and 86`70º E. Nuapadhi village is situated at an altitude of 19 mtrs above sea level. The total area of the study comprised of 438 hectares. The area is usually comprised of tribals belonging to Kolha, Munda & Santhal tribes.

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Temperature ranges between 55°F to 70°F with average rainfall of 10.8 inches.

Data Collection: before data collection the following requirements were ascertained: prior consent of all participants, all participants were either 18 years of age or older and all participants were residents of Nuapadhi village. Data collection was done through semi-structured and structured interviews with participants who knew and/or used plants for medicinal needs. This is a common technique used for ethnobotanical surveys[21]. Interview was conducted with selected informants in their local language. Data was recorded regarding traditional knowledge of utilization of plant species for their medicinal purpose, the utilized plant part and method of preparation or processing of the plant parts. Participants were selected on the basis of Snowball sampling technique for determining the key person[10]. Medicinal plant specimens were collected following standard herbarium procedures and identified using personal expertise and experience as well as by referring published book series of Flora book of Odisha. Photo documentation and herbarium was preserved in the Department of Botany, F M University, Balasore, Odisha.

Disease Classification and Grouping: common hair problems prevalent in the area was categorized

Data analysis: Descriptive analysis was used to tabulate the number as well as percentage of species, genera and families of plants with ethnomedicinal properties, extent of plant parts harvested, plant division to different families, life forms, nature of habitat and plant percentage in treating various hair related ailments.

The quantitative data was subjected to simple linear correlation test to find the correlation between traditional knowledge on medicinal plants and age of informants as well as between medicinal plant knowledge and educational qualification of the informants.

Plant Part Value (PPV): PPV value is calculated as the percentage of plant part (stem, root, leaves, flower, bark, fruit) utilized as biomedical plant resource following the formula of Gomez-Beloz[22].

$$SUV = \frac{\sum RU(plant\ part)}{\sum RU} \times 100$$

Where,
∑RU(plant part) is the sum of the cited plant parts and ∑RU is the sum of total of number of cites used for a given plant.

Species Use Value (SUV): SUV signifies the value of medicinal plant species used by the rural population of Nuapadhi village. It is calculated following the formula as described by Hoffman & Gallaher[23]

$$SUV = \frac{\sum UVis}{(N)}$$

Where,
UVis is the sum of informants who cited the use of particular plant species and N is the total number of informants.

Family Use Value (FUV): FUV was calculated as per the formula as described by Phillips & Gentry[24]. FUV shows the use value of a given plant family used as medicine by the people of Nuapadhi village. FUV value was calculated as per the formula

$$SUV = \frac{\sum UVs}{(N)}$$

Where,
∑UVs represents the summation of the use values of all the species belonging to a particular family and N is the total number of informants.

Fidelity level: the citation of relative frequency was calculated using fidelity level (FL) formula according to[25]. FL is the percentage of informants who claim to use certain plant species or plant parts for any hair problems. It was calculated using the formula:

$$FL(\%) = \frac{Np}{N} \times 100$$

Where,
Np is the number of informants who reported the use of a plant species for treatment of a particular hair problem. N is the total number of informants who reported the use of a plant species for various kinds of hair problems.

RESULTS AND DISCUSSION

Informants` Profile

Table 1: Background of Informants

Variable	Frequency	Percentage
	Sex	
Male	35	35
Female	65	65
Age category		
18-29	11	11
30-39	18	18
40-49	12	12
50-59	28	28
≥60	31	31
Educational background		
Illiterate	17	17
Primary	59	59
Secondary	16	16
Beyond secondary	8	8

Out of the 100 informants interviewed 65 were female and 35 were male (Table 1). The women folk of the area took active interest in profiling the medicinal plants with hair care properties. Elderly people above the age of 60 years category constituted the largest percentage of informants (31%) and the smallest group

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was people of the age group 18-30 (11%). The majority of the population had received only primary education (59%), followed by illiterate (17%), seconday (16%) and beyond secondary (8%). Although the majority of the informants did not have any or much formal education but they are considered as the key repository for traditional knowledge.

Diversity of ethnomedicinal plants and their growth habit as cited by informants

A total of 34 medicinal plants used for treatment of hair problems and belonging to 24 differrent botanical families were recorded from the study area. Plants with medicinal properties used for treating various hair related problems by the people of Nuapadhi village was tabulated along with their family, local name, habitat and plant part used (Table 2). The family with highest number of medicinal plants observed in the study area was Asteraceae (5 members) followed by Rutaceae (3 members), Lamiaceae, Amaryllidacea, Myrtaceae and Fabaceae (all with 2 members each) (Table 2). Similar results showing these botanical families to be rich in medicinal plants have been reported by earlier workers conducting ethnobotanical studies worldwide[26-30]. The above observation is due to the cosmopolitan distribution of these families all over the world[31]. The top botanical family having highest number of medicinal plants validates their efficacy levels by human population all over the world. The utilization of large number of indigenous plant species for curing various hair related problems indicate that the local people still rely on medicinal plants for their primary hair care routine.

Table 2: List of Medicinal Plants and Their Related Information

Botanical/Scientific name of the plant	Family	Vernacular name	Part used	Growth habit	Species Use Value
Hibiscus rosa-sinensis	Malvaceae	Mandara fula	Flowers,leaves	Shrub	1.97
Bacopa monnieri	Plantaginacea	Brahmi	Leaves	Herb	0.5
Aloe barbadensis	Asphodelaceae	Ghee kuari	Gel, leaves	Herb	0.15
Ocimum tenuiflorum	Lamiaceae	Tulsi	Leaves	Shrub	1.88
Trigonella foenumgraecum	Fabaceae	Methi	Seed	Herb	0.34
Cocos nucifera	Arecaceae	Nadia	Fruit	Herb	1.01
Mentha piperita	Lamiaceae	Pudina	Leaves	Herb	0.7
Ricinus communis	Euphorbiaceae	Jada	Fruit	Shrub	0.8
Alium cepa	Amaryllidaceae	Piyaja sandha	Bulb	Herb	0.41
Phyllanthus emblica	Phyllanthaceae	Dhatri aanla	Fruit	Tree	0.79
Allium sativum	Amaryllidaceae	Rasuna sanda	Bulb	Herb	0.11
Rosa indica	Rosaceae	Golapa	Flowers	Shrubs	0.05
Moringa oleifera	Moringaceae	Sajana	Leaves	Tree	1.18
Lawsonia inermis	Lythraceae	Menjuati	Leaves	Tree	0.57
Oryza sativa	Poaceae	Dhana	Fruits	Grass	1.02
Murraya koenigii	Rutaceae	Bhrusunga	Leaves	Shrub	1.5
Citrus limon	Rutaceae	Kagaji lembu	Leaves, Fruits	Tree	0.77
Azadirachta indica	Meliaceae	Neema	Leaves	Tree	1.72
Helianthus annuus	Asteraceae	Suryamukhi	Flowers	Herb	0.91
Tagetes erecta	Asteraceae	Gendu	Flowers	Herb	0.5
Cinnamum verum	Lauraceae	Dalchini	Stem	Tree	0.72
Taraxacum officinale	Asteraceae		Root	Herb	0.89
Nelumbo nucifera	Nelumbonaceae	Padma	Flower	Shrub	0.55
Sapindus mukorossi	Sapindaceae	Ritha	Fruit	Tree	0.92
Acacia concinna	Mimosaceae	Shikakai	Bark,Leaves and Pods	Shrub	0.57
Eclipta prostrate	Asteraceae	Kesarda/ Bhrungaraja	Leaves	Herb	1.02
Centella asiatica	Apiaceae	Thalkudi	Leaves	Herb	1.25
Syzygium aromaticum	Myrtaceae	Labongo	Dried flower bud	Tree	0.83
Musa acuminate	Musaceae	Kadali	Fruit,Stem	Herb	1.74
Milletia pinnata	Fabaceae	Karanja	Fruit	Tree	0.75
Piper betle	Piperaceae	Paana	Leaves	Climber	1.14
Psidium guajava	Myrtaceae	Pijuli	Leaves	Tree	1.33
Aegle marmelos	Rutaceae	Bela	Leaves,Fruit	Tree	1.20
Tridax procumbens	Asteraceae	Bisalyakarani	Leaves	Herb	1.09

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Species use value

In the current study the SUV of the reported plant species ranged between 0.05 to 1.97 (Table2). Five highest SUV was shown by *Hibiscus rosa-sinensis*, *Ocimum tenuiflorum*, *Azadirachta indica*, *Musa acuminate* and *Psidium guajava*. The above data is in accordance with earlier report which showed abundance of the above plant species in the Baleswar district of Odisha. Low SUV was shown by *Mentha piperita*, *Ricinus communis* and *Nelumbo nucifera* with lowest value belonging to *Rosa indica*. The high SUV value may be an indication of over exploitation of a particular plant species as compared to others. On the other hand low SUV value indicates less utilization of the plant which can either be because of lack of knowledge, difficulty in preparation or collection of the plant part used.

Majority of the medicinal plants were collected from wild, and very few were available from home gardens. The present data was in agreement with earlier workers[32,33] which showed most medicinal plants were available in their natural habitat. High availability of medicinal plants in their natural or wild habitat, point out that there is little attempt to conserve or cultivate these plant species by the local population. Thus, the importance of this study lies in the proper documentation of the important ethnobotanical plants and their listing out conservation strategies. Most of the medicinal plants were herbs (41.17%) followed by tress (32.35%) and shrubs (20.58%) (figure 1).

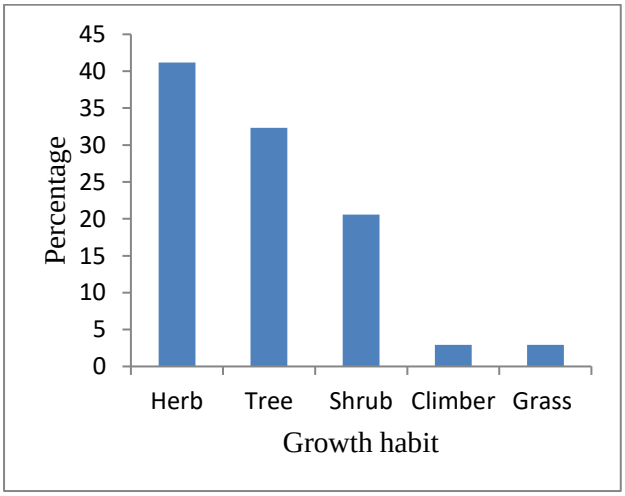

Figure 1: Growth Habit of Medicinal Plants Used to Treat Hair Related Problems in The Study Area

Plant Part Used, Method of Preparation, Dosage and Administration

The people of the study area harvested different parts for different plant species to extract the phytochemical ingredient for medicinal purpose. Plant parts have the potential to store active phytochemical substances that are valuable from pharmaceutical aspect. In the present study, leaves (42.5%) were observed to be most effective for treatment of hair diseases followed by fruits (22.5%) and flowers (5%) (figure 2). Earlier workers have also reported that leaves are primarily used for medicinal preparations[34-36]. Calculating Plant Part Use is a functional method to ascertain the major plant part used for medicinal cause[37]. Leaves are most commonly used plant part world over for preparation of medicinal products because of their easy handling and sustainability. Removing leaves from plants is less damaging for the plant species as compared to roots, fruits or flowers. The mode of preparation of plant extracts for treating hair problems is shown in (table 3). Preference of extracting leaves over roots or barks can be attributed to simplicity of preparation of medicinal concoction. Moreover plants are the site of photosynthesis and therefore accumulate secondary metabolites[38-40].

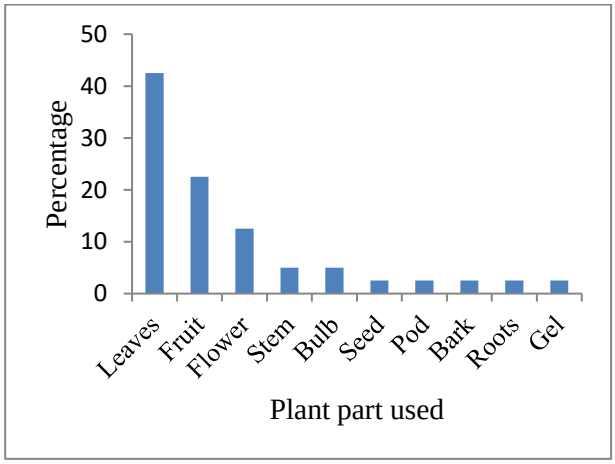

Figure 2: Plant Part of Medicinal Plants Used to Treat Hair Related Problems in The Study Area

The preparation technique for hair care products indicated vast knowledge of the local people about the medicinal properties of these plant species. Informants of different ethnic communities from the study area revealed various monoherbal and polyherbal preparations were used for various medical treatments (Table 2). Similar research findings reporting use of single plant species or plant parts for preparing traditional remedies is available in literature[41,42]. The current study revealed that the people from Nuapadhi village preferred using mixture of different plant parts to heal hair problems can be a result of years of experience and understanding. As per the informants interviewed from the present study area of Nilagiri village, grinding appeared to be the most popular method used for harvesting plant parts for their bioactive components (Table 3). The second most popular method was preparation of paste followed by crushing the dried leaves and applying them raw as well as mixing the extract with coconut oil. The observed result is in concurrence with other reports where grinding was observed to be the most preferred method for preparation of traditional medicinal products[43-45]. The inclination of using fresh plant parts as compared to dried plant parts for preparing medicinal product may point towards the

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belief of the rural people that maximum extraction is possible in fresh plant parts and some of the effectiveness is lost when the plant part in dried. Such observation from different ethnic communities around the world have been reported earlier[46, 47]. The preferred method of application of hair care product was direct application on the scalp (table 3), followed by applying it on the whole hair and hair mask. Further the same preparation was prescribed in different doses to people according to the hair problem, sex and age of the respondent. Recovery from the disease depended on the cessation of the disease symptom and/or judgement of the user or the healer.

Table 3: Method of preparation and application of the medicinal plants

Scientific name	Method of preparation and application
Hibiscus rosa-sinensis	Grinding the flower and leaves with yoghurt and coconut oil
Bacopa monnieri	Making a paste of the leaves
Aloe barbadensis	Gel from the leaves are applied directly or along with coconut hair oil
Ocimum tenuiflorum	Leaves are crushed and applied onto the scalp
Trigonella foenumgraecum	Grinding and can be applied alone or with oil
Cocos nucifera	Oil
Mentha piperita	Making a paste applying with coconut oil
Ricinus communis	Oil
Alium cepa	Grinding and applied with and without oil
Phyllanthus emblica	Oil and powder is used to make a smooth paste and applied onto scalp
Allium sativum	Grinding and applied with and without oil
Rosa indica	Grinding of petals
Moringa oleifera	Dry grinding to make powder
Lawsonia inermis	Leaves are grinded to make a paste and applied with lemon juice
Oryza sativa	Rice water
Murraya koenigii	Leaves are boiled to get the extract and then applied onto scalp
Citrus limon	Lemon juice
Azadirachta indica	Dry leaves are grinded to make powder. Leaves are used to prepare paste by boiling them in water.
Helianthus annuus	Oil
Tagetes erecta	Oil
Cinnamum verum	Oil
Taraxacum officinale	Paste
Nelumbo nucifera	Juice is extracted by grinding or heating
Sapindus mukorossi	The seeds are dry grounded to get the powder and then mixed with water to prepare a paste and then applied
Acacia concinna	Dry grounded to get the powder and then mixed with water to prepare a paste and then applied
Eclipta prostrate	Oil
Centella asiatica	It is taken as salad or used to make tea
Syzygium aromaticum	Oil
Musa acuminate	The fruit is mashed and applied all over hair
Milletia pinnata	Oil
Piper betle	Beetle leaves and ginger is added in an iron vessel with coconut oil and heated on low flame. After cooling applied on the hair
Psidium guajava	Leaves are boiled with water until it changes colour. After the mixture cools is used to massage scalp
Aegle marmelos	Dry leaf is grounded and mixed with coconut oil on scalp
Tridax procumbens	Leaves are used to make a paste and applied on the scalp

Relationship Between Age of Informant and Their Knowledge of Traditional Medicinal Plants

Pearson co-relation co-efficient used to analyse the association between the age of the informants and their medicinal plant knowledge revealed a positive correlation (r=0.952) (figure3). The elderly people possessed more knowledge about the traditional ways of utilizing medicinal plants as compared to younger generation. In agreement to the present study various studies have showed that as people get older their understanding of the medicinal plants enriches and enhances[48,49]. On the other hand lack of information in the younger population could be a result of improper transfer of information from the elders. Moreover the present day pressure created by commercial products readily available may have created an aversion towards these natural remedies.

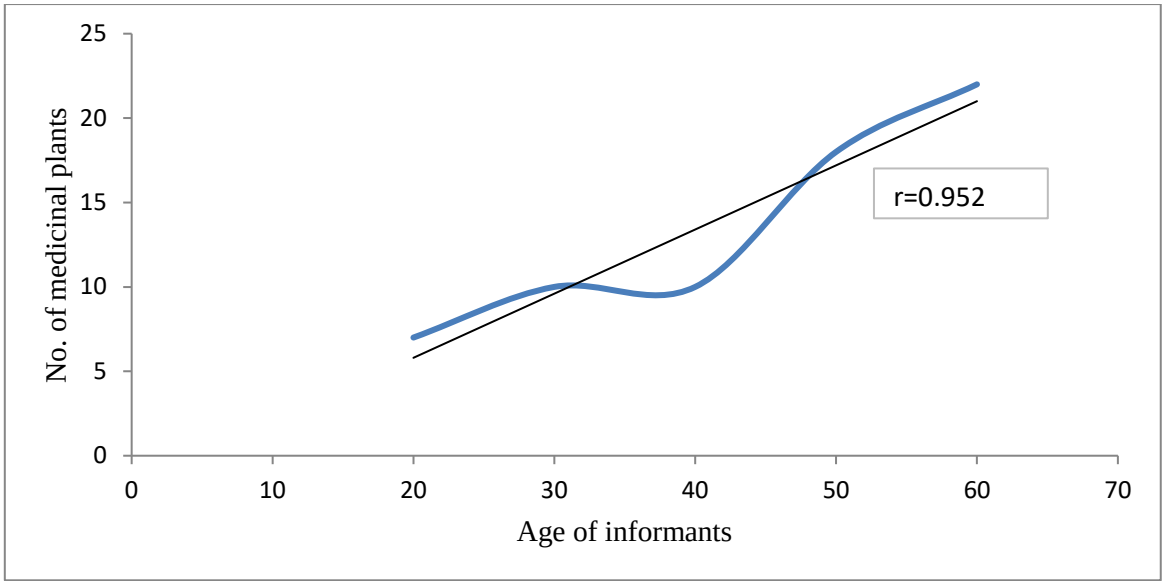

Figure3: Age of the Informants Versus Number of Medicinal Plants Cited by Them from The Study Area

Relationship Between Educational Level of Informant and Their Knowledge of Traditional Medicinal Plants

Pearson correlation analysis was carried out to determine the relationship between level of education of the informants and their traditional medicinal plant knowledge revealed a positive correlation (r=0.87) (figure4). Although other workers have showed a negative correlation[50], the informants belonging to tribes of the Nuapadhi village showed a positive association. The present result can be a cause of the social framework of the village culture where people live in joint families with their elders and have a respect for their customs and traditions.

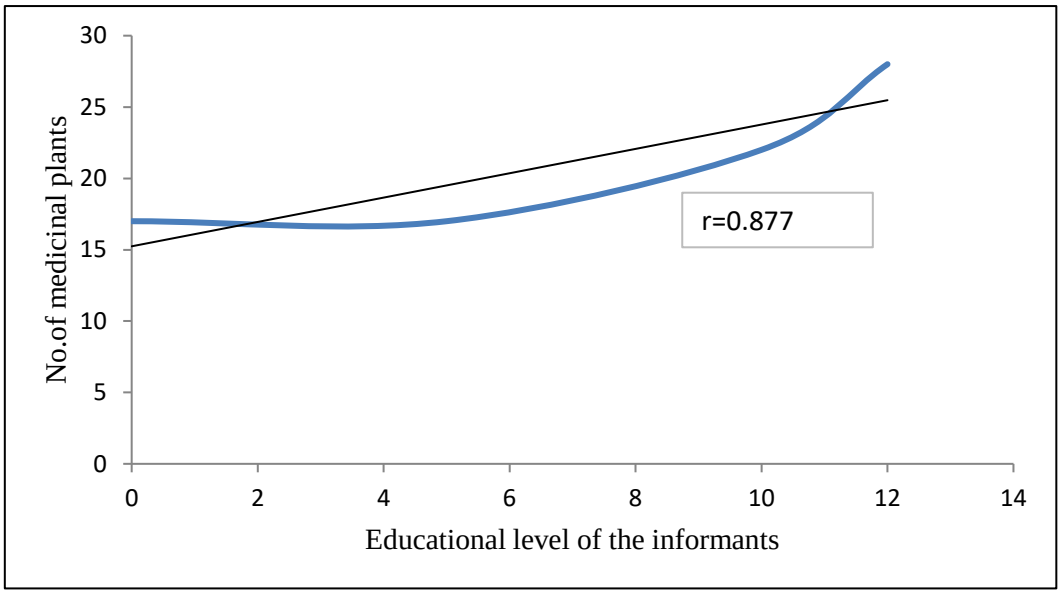

Figure 4: Age Versus Educational Level of The Informants from The Study Area

Family Use Value

In the present study a total of 24 families were observed with Asteraceae being the most dominant one (table 4). The abundance of Asteraceae family with maximum representation of plant species with medicinal properties is due to high accessibility of the plant in the study area. The high availability of the particular species can be attributed to the climatic and environmental conditions of the area which is favourable for the growth of the plant. This also proves that the dominantly available plant or plant family is often targeted by the local people to cure different ailments. The total number of species belonging to the same family was used to calculate the FUV. In the present work Asteraceae showed highest FUV value followed by Fabaceae, Rutaceae and Phyllanthaceae (table 4). High FUV for a specific plant family was due to more informant citing the plant species belonging to that botanical family. Similar results have been reported from other countries[51-55].

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Table 4: Distribution of The Medicinal Plant Species Among the Plant Families, Percentage of Distribution and Family Use Value (FUV)

Family	Number of plant species	Percentage	FUV
Asteraceae	5	14.70588	0.89
Rutaceae	3	8.823529	0.51
Lamiaceae	2	5.882353	0.19
Amaryllidacea	2	5.882353	0.08
Myrtaceae	2	5.882353	0.14
Fabaceae	2	5.882353	0.73
Malvaceae	1	2.941176	0.08
Plantaginacea	1	2.941176	0.5
Asphodelaceae	1	2.941176	0.04
Arecaceae	1	2.941176	0.9
Euphorbiaceae	1	2.941176	0.31
Phyllanthaceae	1	2.941176	0.2
Rosaceae	1	2.941176	0.06
Moringaceae	1	2.941176	0.01
Lythraceae	1	2.941176	0.5
Poaceae	1	2.941176	0.07
Meliaceae	1	2.941176	0.3
Lauraceae	1	2.941176	0.01
Nelumbonaceae	1	2.941176	0.09
Sapindaceae	1	2.941176	0.05
Mimosaceae	1	2.941176	0.17
Apiaceae	1	2.941176	0.19
Musaceae	1	2.941176	0.08
Piperaceae	1	2.941176	0.01

Fidelity Level

FL is a representation of the percentage of informants who cited the use of the same plant species for the same problem. As per Imran *et al*[56] FL is crucial for determining the level of species importance in reference to a specific disease. The results from the present study area revealed that FL% of the 34 medicinal plant species belonged between 1.09 to 89.96 (Table 5). *Hibiscus rosa-sinensis* revealed highest FL for hair problem, followed by *Sapindus mukorossi* and *Trigonella foenumgraecum*. Previous study have showed that high FL act as bio-pharmacological marker and prompt scientist to undertake further conservation strategies and phytopharmacological analysis[57]. Lowest FL value was shown by *Tridax procumbens*. Difference in FL among plant species is caused due to difference in their abundance and growth pattern in the study area.

Table 5: Fidelity Level of Medicinal Plants from The Study Area

Disease	Plant species	Fidelity level (%)
Dryness, Dandruff	*Hibiscus rosa-sinensis*	89.96
Hair loss, Dandruff	*Bacopa monnieri*	47.11
Hair loss, Dandruff	*Aloe barbadensis*	51.91
Hair loss, Dandruff, pre-mature graying	*Ocimum tenuiflorum*	38.84
Lice treatment, Hair Fall, Dandruff	*Trigonella foenumgraecum*	71.15
Baldness, Hair growth, Scalp treatment	*Cocos nucifera*	28.84
Baldness, Hair loss	*Mentha piperita*	3.58
Hair loss	*Ricinus communis*	30.67
Baldness, Hair re-growth	*Alium cepa*	21.15
Hair loss, pre-mature graying	*Phyllanthus emblica*	11.50
Hair Fall, Dandruff	*Allium sativum*	3.38
Scalp infection, Dandruff	*Rosa indica*	1.92
Hair loss	*Moringa oleifera*	3.50
Hair Fall, Hair Dryness, Dull Hair	*Lawsonia inermis*	50.56
Rough and Frizzy Hair	*Oryza sativa*	1.92
Scalp treatment	*Murraya koenigii*	15.30
Scalp treatment, Dandruff	*Citrus limon*	36.53
Dandruff, Lice Treatment	*Azadirachta indica*	11.18
Hair loss, Dandruff	*Helianthus annuus*	3.21
Hair loss	*Tagetes erecta*	1.52
Hair loss, Dandruff	*Cinnamum verum*	1.30
Hair Fall	*Taraxacum officinale*	2.18
Dull Hair	*Nelumbo nucifera*	42.30
Hair loss, Dandruff, Dull Hair	*Sapindus mukorossi*	79.69
Hair Cleanser, Hair Shine, Dandruff, Lice Treatment	*Acacia concinna*	44.75
Hair Fall, Dandruff, Pre-mature graying	*Eclipta prostrate*	66.14
Pre-mature graying	*Centella asiatica*	21.09
Hair Fall, Dandruff, Pre-mature graying	*Syzygium aromaticum*	33.70
Rough and Frizzy Hair, Dandruff	*Musa acuminate*	3.89
Damaged and Frizzy hair treatment	*Milletia pinnata*	1.90
Hair Fall	*Piper betle*	1.43
Hair Fall	*Psidium guajava*	17.62
Hair Fall	*Aegle marmelos*	3.91
Hair Fall	*Tridax procumbens*	1.09

CONCLUSION

The result in the present work highlighted the use of medicinal plants by the rural people of Nuapadhi village for curing of hair problems A total of 34 species were identified belonging to 24 families. This reflected the high diversity of plants in the area as well as focused on the rich local knowledge of the in terms of traditional medicinal plants. The species use value, family use value and fidelity value presented in this paper can be used by conservationist to strategize future road map for conservation and protection of the important plant species. Further this data can be employed for further pharmacological studies and new drug delivery.

Popularizing and marketing the use of these herbal products can enable the local communities earn profit and significantly improve the economic status of the local community as well bring revenue for the Government.

Conflict of interest: No conflict of interest exists between the authors.

Author contribution: All authors have contributed equally.

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