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Review

Traditional uses of medicinal plants in gastrointestinal disorders in Nepal

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ABSTRACT

Ethnopharmacological relevance: Gastrointestinal disorders cause morbidity and can lead to mortality, especially in the developing world where sanitation is deficient. A large part of the human population relies on medicinal plants for treating various diseases, including gastrointestinal disorders. The present review summarizes the traditional uses of medicinal plants of Nepal used to treat gastrointestinal disorders, and evaluates their bio-efficacy based on a review of the available phytochemical and pharmacological literature.

Material and methods: We searched different electronic databases and libraries for the literature on medicinal plants used in Nepal to treat gastrointestinal disorders. For each species, we also searched the literature for information on conservation status, as well as for phytochemical and pharmacological studies in support of the ethnobotanical information. We used principal component analysis to explore the relation among disorders and plant families, plant life forms, plant parts and preparation modes. We also performed permutation tests to determine if botanical families were used more often than expected considering their availability in the Nepali flora.

Results: We documented a total of 947 species belonging to 158 families and 586 genera used to treat gastrointestinal disorders in Nepal. Diarrhea was the disorder treated by the highest number of species (348), followed by stomachache (340) and dysentery (307). Among the reported species, five were endemic to Nepal, whereas 16 orchid species were protected under CITES Appendices II and III. The randomization test showed that species belonging to 14 families were used less often than expected, whereas plants belonging to 25 families were used more often than expected. The PCA scatter plot showed distinct groups of gastrointestinal disorders treated with similar plant life forms, plant parts, and/or preparation modes. We found 763 phytochemical studies on 324 species and 654 pharmacological studies on 269 species.

Conclusion: We showed the diversity and importance of medicinal plants used to treat gastrointestinal disorders in the traditional health care system of Nepal. As such disorders are still causing several deaths each year, it is of the utmost importance to conduct phytochemical and pharmacological studies on the most promising species. It is also crucial to increase access to traditional medicine, especially in rural areas. Threatened species need special attention for traditional herbal medicine to be exploited sustainably.

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Contents

1. Introduction . . . 222
2. Material and methods . . . 222
2.1. Data collection . . . 222
2.2. Data analysis . . . 223
3. Results . . . 224
3.1. Diversity, uses, preparation modes . . . 224
3.2. Ethnicities, districts and regions . . . 225
3.3. Pharmacological and phytochemical evidences . . . 225
3.4. Multiple-use species . . . 225
3.5. Conservation status . . . 226
4. Discussion . . . 226
4.1. Diversity, uses, preparation modes . . . 227
4.2. Efficacy of medicinal plants. . . . 227
4.3. Implications for primary health care, bio-prospecting and drug development . . . 227
4.4. Conservation status of medicinal plants . . . 228
5. Conclusion . . . 228
Acknowledgments . . . 228
Appendix A. Supporting information . . . 228
References . . . 228

1. Introduction

It is estimated that 70–80% of the human population, mostly in the developing world, relies on medicinal plants for primary health care (WHO, 2008). Herbal medicines are also gaining popularity among the western population because they have minor or no side effects if administered properly (Jordan et al., 2010). Besides medicinal use, plants are increasingly used in cosmetics (Aburjai and Natsheh, 2003) and nutraceutics (Espín et al., 2007; Bernal et al., 2011). Herbal medicines have been proved to be highly effective to treat a wide range of diseases (Blumenthal, 2002; Mukherjee and Wahile, 2006), including gastrointestinal disorders (Heinrich et al., 1992; Manandhar, 2002; Madikizela et al., 2012; Street and Prinsloo, 2013).

Gastrointestinal disorders are ailments affecting the functions of the digestive tract, i.e., food and liquid absorption, digestion, or excretion (Neamsuvan et al., 2012). Such disorders are caused by infections by various kinds of bacteria, viruses, and parasitic organisms (Mathabe et al., 2006; Karki and Tiwari, 2007). Common gastrointestinal disorders are stomach/abdominal pain, diarrhea, dysentery, gastroenteritis, constipation, vomiting, etc. (WHO, 2008). These disorders cause morbidity and can lead to mortality, especially in the developing world where sanitation is deficient (Heinrich et al., 1992; Pawlowski et al., 2009; Tuite et al., 2011). Outbreaks of diarrhea, dysentery, or cholera caused by contaminated drinking water have claimed millions of lives worldwide, mainly infants and children (Sarkar et al., 2007; Ryan, 2011). For example, serious diarrhea/dysentery/cholera outbreaks were reported in Ethiopia (Bartels et al., 2010), Haiti (Tuite et al., 2011), Vietnam (Anh et al., 2011), Zimbabwe (Fisher, 2009), and Nepal (Bhandari et al., 2009), all with a high death toll.

In Nepal, 80–85% of the population depends on traditional medicine for primary health care (Manandhar, 2002). The use of medicinal plants is widespread, not only because they are easily accessible and affordable, but also due to persistent cultural beliefs and practices, as well as the lack of access to modern health care systems in rural areas (Coburn, 1984; Pohle, 1990; Baral and Kurmi, 2006). Medicinal plants are used to treat various gastrointestinal disorders ranging from simple types such as vomiting to more complex problems like peptic ulcer (Lama et al., 2001; Rajbhandari, 2001).

There are many studies related to traditional uses of plant species in Nepal (Manandhar, 2002; Shrestha et al., 2004; Joshi and Joshi, 2005; Kunwar and Bussmann, 2008). Besides ethnobotanical studies, in-vitro and in-vivo trials were realized to identify the mechanisms explaining the effectiveness of some of the medicinal plants used in traditional medicine (Griggs et al., 2001; Panthi and Chaudhary, 2006; Rajbhandari et al., 2009). This practice of establishing phytochemical or pharmacological explanations for traditional uses is not only helpful to institutionalize traditional medicine, but can also lead to the development of new drugs (Newman and Cragg, 2007) or indicate future directions for bio-prospecting (Soejarto et al., 2005; Douwes et al., 2008). However, only a few studies have so far linked traditional medicinal uses to pharmacological or phytochemical properties in Nepal (Kunwar et al., 2009; Uprety et al., 2010; Gaire and Subedi, 2011; Luitel et al., 2014).

The present study aimed at documenting the traditional uses of medicinal plants to treat gastrointestinal disorders in Nepal, and to evaluate the efficacy of plant species based on a review of the literature. Specifically, we sought to answer the following questions: (i) What plant species are used in gastrointestinal disorders in Nepal? (ii) Have pharmacological or phytochemical studies been conducted to determine which metabolites are active against gastrointestinal disorders? (iii) What gastrointestinal disorders are treated with the highest number of medicinal plant species? (iv) Are some botanical families more or less used than expected in gastrointestinal disorders? and (v) Which diseases are commonly treated by which plant parts, plant types, modes of admission, and botanical families?

2. Material and methods

2.1. Data collection

We reviewed studies published in journals, reports and books dealing with traditional uses of medicinal plants in Nepal to treat various gastrointestinal disorders. Different online databases were used (ISI Web of Science, MEDLINE, Science Direct, Scopus, and Google Scholar), with specific search terms such as 'medicinal plants', 'plants', 'gastrointestinal', 'gastro', 'diarrhea', 'dysentery', 'stomach' and 'Nepal' (for all terms see Table 1). The term 'Nepal' was used to limit the geographical scope of the search. We also carried out library search for hard copies. We reviewed a total of 94 publications. A master list was produced, providing vernacular name(s), mode(s) of use, and references for each species (Electronic Appendix 1).

The precision of species names provided in this paper depends on that from the original sources. However, we verified currently accepted name(s) in Press et al. (2000) and online nomenclature sources (http://www.theplantlist.org and http://www.tropicos.org). The currently accepted name is sometimes followed by synonyms, when provided in the source references. Available vernacular names are also provided. The most frequently used plants were identified based on the highest number of use reports from the literature. Life forms and origin (wild/cultivated) of the different plant species were noted if mentioned in the original documents, otherwise we used other sources of information (Polunin and Stainton, 1984; Stainton, 1988; Storrs and Storrs, 1998; Lama et al., 2001; Manandhar, 2002; Baral and Kurmi, 2006).

We searched the above-mentioned databases for pharmacological or phytochemical studies providing supporting evidence of medicinal uses for each species. Pharmacological studies show direct explanation for traditional uses, whereas phytochemical studies provide indirect information. Plants contain several types of secondary metabolites that have different therapeutic properties. We did not restrict the search to Nepal, as species might have been tested elsewhere. Due to the huge number of studies having been consulted, we only provide the reference(s), and complete information on pharmacological and phytochemical properties can be retrieved from the original studies. We provide a complete set of references in Electronic Appendix 1.

Table 1
Number of plant taxa used to treat various gastrointestinal disorders.

Disorder	Abbreviation(s)	No. of plant taxa[a]
Diarrhea	Dia	348
Stomachache	Sto	340
Dysentery	Dys	307
Indigestion/Digestion/Digestive	Ind	303
Constipation/Laxative/Purgative	Con lax	221
Anthelmintic	Ant	175
Gastritis	Gas	173
Hepatoprotective/Jaundice	HepJau	127
Appetizer	App	102
Colic	Col	85
Bile disorder	Bil dis	72
Emetic/Vomiting/Nausea	EmeVom	70
Carminative/Flatulence/Tympanite	Car	67
Piles	Pil	52
Ulcer	Ulc	46
Splenopathy	Spl	37
Cholera	Cho	34
Intestinal disorder	Ind dis	21
Other diseases	Oth dis	16
Astringent	Ast	9

[a] A taxon may be used to treat more than one disorder.

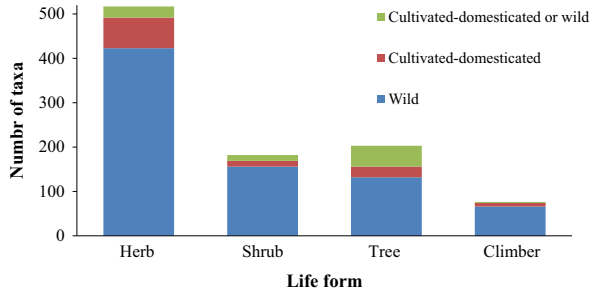

Fig. 1. Frequency distribution of medicinal plant taxa according to life form and origin (wild, cultivated or both).

2.2. Data analysis

We categorized gastrointestinal disorders into 20 categories following the classification of Cook (1995) (Table 1). Categories consisting of similar disorders or physiological effects of medicinal plants were grouped, such as carminative/flatulence/tympanites, constipation/laxative/purgative, emetic/nausea/vomiting, hepatoprotective/jaundice, and indigestion/digestion/digestive. An 'other diseases' category was created, consisting of diseases not included into other categories: somatosis, enteritis, swollen stomach, food poisoning, pharyngitis, colon carcinoma proliferation and inflammation of the intestinal membrane.

The conservation status of plant species was determined using the available data in Conservation Assessment and Management Prioritization report (CAMP, 2001), International Union for Conservation of Nature (IUCN, 2013), Government of Nepal (GoN/MoFSC, 1995, 2006), Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES, 2013), endemic plant list of Nepal (Shrestha and Joshi, 1996), and highly traded plant species of Nepal (ANSAB, 2013).

We applied data reduction methods to summarize the data. Principal component analysis (PCA) was used to determine which gastrointestinal disorders (dependent variable) were treated with particular combinations of plant life forms, plant parts, or preparation modes (independent variables) (Lepš and Šmilauer, 2003). PCA was also used to verify which types of gastrointestinal

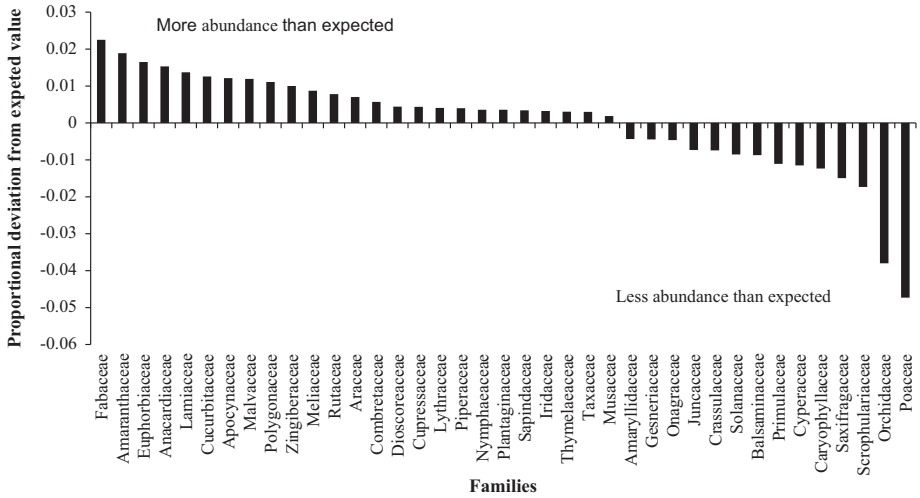

Fig. 2. Proportional deviation of medicinal plants used in gastrointestinal disorders compared to total abundance of vascular plants. Only significant deviations are shown.

disorders were treated with the same plant families. PCA was carried out using Canoco 5.01 (ter Braak and Smilauer, 2012).

We first counted the number of species in each family among the species used to treat gastrointestinal diseases. A high number of species in a given family may, however, have two explanations: the given plant family might have properties making it a valuable source of medicine, or it might only be common in the area. To explore these two possibilities, we tested if some botanical families had more species used in gastrointestinal diseases than expected from the total number of species in each family in the flora of Nepal (Press et al., 2000). Specifically, we tested whether the plants used in gastrointestinal diseases were random subsets of all vascular plants and all medicinal plant species regarding identity to botanical family, following the method described in Rokaya et al. (2012b). For this, we performed permutation tests by drawing random samples of plants from the whole flora of Nepal and assigning them to plant families. We asked whether the number of species used in gastrointestinal diseases in a given family could result from a random sampling from the whole flora or from the medicinal flora of Nepal. For each family, we derived an empirical *P*-value, which indicated the probability that the number of species of a given family used to treat gastrointestinal diseases could be due to random sampling from the total flora or medicinal flora of Nepal. We performed 10,000 permutations using MATLAB 5.3 (1999).

3. Results

3.1. Diversity, uses, preparation modes

A total of 947 species belonging to 158 families and 586 genera were reported in the literature as being traditionally used in Nepal to treat different gastrointestinal ailments. Most of the reported medicinal plant species were Angiosperms (892 species: 777 Dicotyledons and 115 Monocotyledons). Pteridophytes ranked second (37 species), followed by Gymnosperms (16 species). Well represented Angiosperm families were Fabaceae (72 species), followed by Asteraceae (55), Lamiaceae (39), Rosaceae (32) and Ranunculaceae (31). *Aconitum*, *Desmodium*, *Phyllanthus* and *Swertia* were the most common genera representing 8 species, followed by *Allium*, *Amaranthus*, *Arisaema*, *Delphinium*, and *Potentilla* with 7 species. The highest prevailing life form was herb (486 species), and most remedies were prepared from wild plant species (755 species) (Fig. 1). The nomenclature used in the consulted publications was different from the current accepted nomenclature for 53 plant species. We included these names as synonyms in our database.

The randomization test with all the vascular plants of Nepal showed that species belonging to 14 families were used less often than expected (e.g., Poaceae, Scrophulariaceae, Caryophyllaceae, etc.), whereas plants belonging to 25 families were used more often than expected in gastrointestinal diseases (Fig. 2). Considering only the medicinal flora, plant species belonging to six families were used less often than expected and plants from seven families were used more often than expected in gastrointestinal disorders (Fig. 3).

The reported plants were used in 20 different gastrointestinal ailment categories (Table 1). Diarrhea was the disorder treated by the highest number of species (348), followed by stomachache (340) and dysentery (307). Two-thirds of the species (65.96%) were used to treat more than one ailment, whereas 34.04% were used to treat a single ailment (Electronic Appendix 1).

Almost all plant parts were used to prepare different medicinal formulations: roots/rhizomes/bulbs/tubers/corm/cloves, fruits/seeds/pulp, leaves/petiole, stem/wood, bark, flowers/buds, gum/sap/latex/milk/resin and whole plant. The most frequently used plant parts were the underground parts followed by fruits/seeds (Fig. 4). Paste was the most frequently used preparation technique, followed by decoction and powder (Fig. 5). As gastrointestinal disorders are related to internal body parts, most medicinal formulations were consumed orally, often with water and sometimes with milk and honey. It was also reported that leaves of some species, such as *Artemisia dubia*, were put over a heated flat stone on which patients would sit or lie to treat common-dysentery or blood-dysentery.

The first axis of the PCA of disorders in relation to plant parts, plant types and modes of preparation explained 58.59% of the variance in treated disorders. It separated modes of preparation, with plants ingested raw, or as juice or soup on one side, and plants applied or ingested using more elaborate preparations on the other side (Fig. 6). The second axis explained 17.58% of the variance and separated trees and shrubs on one side, from herbs, climbers and fungi on the other side. Powder and decoction from underground

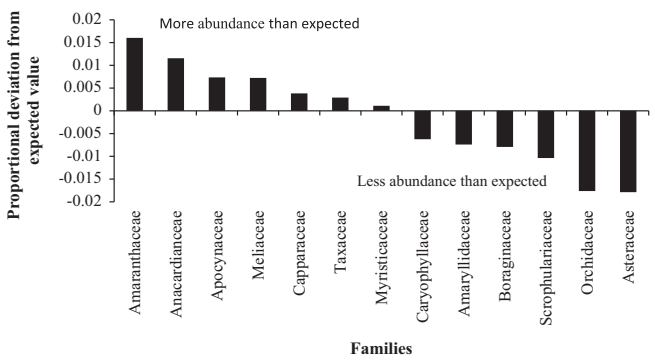

Fig. 3. Proportional deviation of medicinal plants used in gastrointestinal disorders compared to total abundance of medicinal plants. Only significant deviations are shown.

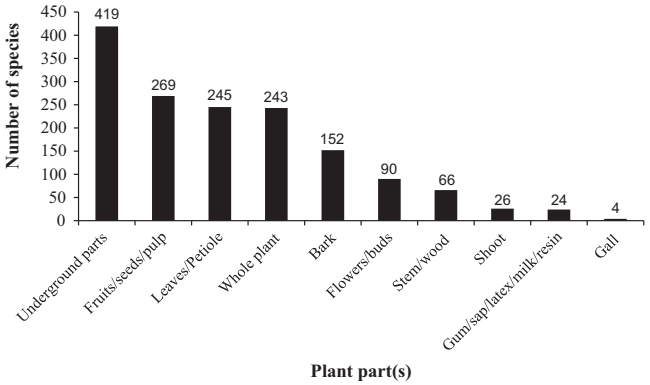

Fig. 4. Use frequency (number of species) of different plant parts.

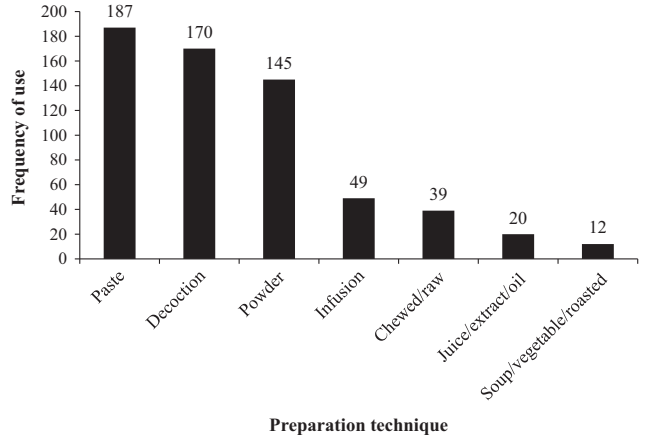

Fig. 5. Use frequency of remedy preparation techniques.

parts and flowers of shrubs were used as anthelmintic, appetizer or in bile disorder. Juice, soup/vegetables from herbs were used for several disorders, including indigestion/digestion, diarrhea, intestinal disorder, hepatoprotective/jaundice, constipation/laxative/purgative, splenopathy, emetic/vomiting/nausea and ulcer. Paste from gum or fungi was used in colic (Fig. 6).

A PCA was also realized to examine the relation between diseases and botanical families. Species from the Valerianaceae family was used for emetic/vomiting/nausea. Species from the Nymphaeaceae, Sapotaceae, Brassicaceae, Myrtaceae and Clusiaceae families were used as astringent. Species from the Taxaceae and Apiaceae families were used as carminative/flatulence/tympanite. Species from the Fabaceae and Malvaceae families were used in bile disorders, constipation and splenopathy. Species from the Rosaceae and Poaceae families were used in dysentery and diarrhea. Species from the Euphorbiaceae and Asteraceae families were used in hepatitis/jaundice and as anthelmintic. Species from the Ranunculaceae family was used in stomachache, internal disorders, indigestion, gastritis, and ulcers (Fig. 7).

3.2. Ethnicities, districts and regions

The different studies reviewed were carried out from 15 different ethnic communities (Bankariya, Bantar, Chepang, Darai, Gurung, Limbu, Magar, Meche, Newar, Rai, Raji, Satar, Sherpa, Tamang and Tharu) from nine areas (Bagmati zone, central Nepal, far west Nepal, Karnali zone, Khaptad National Park, Rapti zone, Panchase region, Rolwaling region and Kali Gandaki watershed area) and 35 districts in Nepal. There were more studies from central Nepal compared to other areas. The earliest studies we found were published in 1974 and the year with the most studies published was 2000.

3.3. Pharmacological and phytochemical evidences

We found slightly more phytochemical studies (763 studies for 324 species) than pharmacological studies (654 studies for 269 species) on plant species used in gastrointestinal disorders in Nepal (Electronic Appendix 1). We found both types of studies for 126 plant species. More pharmacological studies were in-vivo experiments (249) than in-vitro experiments (178). Almost all in-vivo experiments were conducted for diarrhea, induced in Wistar rats by castor oil and magnesium sulfate, *Escherichia coli* enterotoxin, charcoal meal, castor oil-arachidonic acid, and prostaglandin (PGE). The in-vitro experiments included antimicrobial tests for diarrhea or dysentery or for other diseases caused by bacteria such as *Escherichia coli*, *Shigella* spp., *Salmonella typhii*, *Vibrio cholera*, *Pseudomonas aeruginosa* and *Aeromonas hydrophyla*. Species from the Fabaceae, Lamiaceae and Asteraceae families were highly investigated, both for pharmacological bioassays and phytochemical studies.

Plant species with various kinds of secondary metabolites such as alkaloids, amino acids, tannins, terpenes, steroids and flavonoids (e.g., *Abrus precatorius*); fatty acids, sugars, asarone, sequestrine ketones (e.g., *Acorus calamus*); artemisia ketone, germacrene B, borneol and cis-chrysanthenyl acetate (e.g., *Artemisia indica*); flavonoid glycoside, flavinoids, pyrrolidine (e.g., *Drymaria diandra*, *Lobelia chinensis*), emodin (e.g., *Rheum australe*); phenolic acids (*Terminalia* species); sterols, lactones and glycosides (e.g., *Tinospora cordifolia* and *Withania somnifera*) were used to treat gastrointestinal disorders, mainly diarrhea and dysentery.

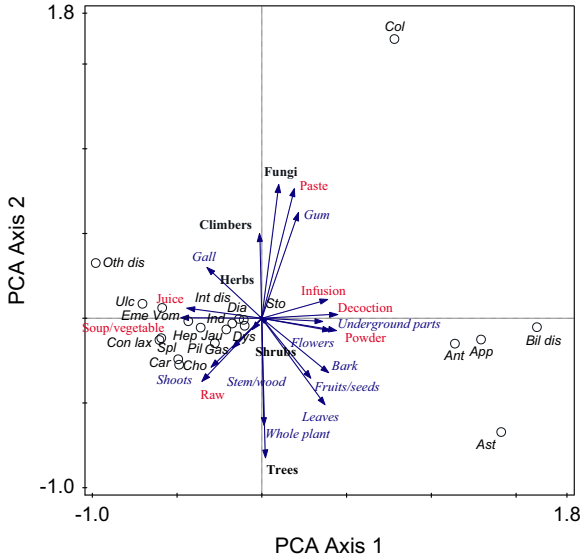

Fig. 6. Principal component analysis (PCA) showing different gastro-intestinal disorders (circles), plant parts (in blue), preparations (in red) and life forms (in bold black). The first and second axes respectively explained 58.59% and 17.58% of the variability in the total dataset. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
Abbreviations: Ant—Anthelmintic; App—Appetizer; Ast—Astringent; Bil dis—Bile disorder; Car—Carminative/Flatulence/Tympanite; Cho—Cholera; Col—Colic; Con lax—Constipation/Laxative/Purgative; Dia—Diarrhea; Dys—Dysentery; EmeVom—Emetic/Vomiting/Nausea; Gas—Gastritis; HepJau—Hepatoprotective/Jaundice; Ind dis—Intestinal disorder; Ind—Indigestion/Digestion/Digestive; Pil—Piles; Spl—Splenopath; Sto—Stomachache; Ulc—Ulcer; Oth dis—Other diseases.

3.4. Multiple-use species

A total of 35 species were reported to treat more than eight different gastrointestinal disorders (Table 2). A few species were reported to treat more than 10 disorders (*Bombax ceiba*, *Chenopodium album*, *Cinnamomum tamala*, *Oxalis corniculata*, *Phyllanthus emblica* and *Psidium guajava*).

Out of the 35 plant species used to treat the most different disorders, pharmacological studies were available for 27 and phytochemical studies for 32 species (Table 2). Species for which no pharmacological studies were available were *Catunaregam spinosa*, *Curculigo orchioides*, *Euphorbia royleana*, *Juniperus indica*, *Nardostachys grandiflora*, *Rubia manjith* and *Thymus linearis*, whereas species

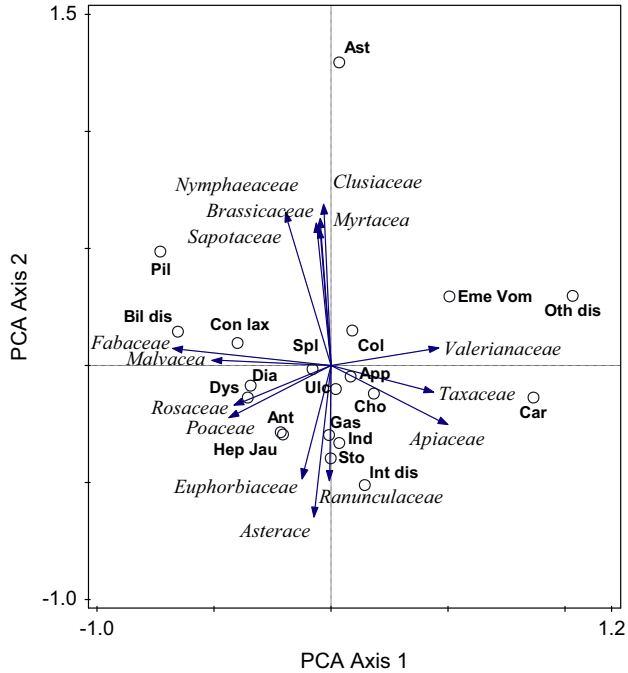

Fig. 7. Principal component analysis (PCA) showing relationship between diseases and twenty highly used families. The first and second axes respectively explained 18.02% and 15.02% of the variability in the total dataset.

Table 2
Plant species used for at least 8 different purposes.

Plants species	Disorders
Achyranthes aspera	Astringent, cholera, constipation, diarrhea, dysentery, laxative, loss of appetite, nausea, stomach disorders, stomachache and vomiting.
Acorus calamus	Anthelmintic, bowel, cholera, colic, diarrhea, dysentery, dyspepsia, stomach disorders and stomachache.
Aegle marmelos	Abdominal disorders, amebic dysentery, astringent, carminative, colic, constipation, diarrhea, digestive, dysentery, gastritis, indigestion, intestinal disorder, laxative and stomachache.
Allium cepa	Colic, constipation, dysentery, dyspepsia, hepatopathy, indigestion, splenopathy, stomach disorders, stomachache and vomiting.
Aloe vera	Constipation, dysentery, hemorrhoids, hepatic stimulant, indigestion, intestinal worms, liver disorders, spleen enlargement, peptic ulcer, stomach disorders and stomachache.
Alstonia scholaris	Anticholeric, constipation, diarrhea, digestive, dysentery, dyspepsia, laxative, stomachic and vermifuge.
Asparagus racemosus	Appetizer, biliousness, constipation, diarrhea, dysentery, dyspepsia, flatulence, laxative, stomach disorders and stomachache.
Bergenia ciliata	Abdominal spasm, antiemetic, anthelmintic, bile disorders, diarrhea, dysentery, gallstone, gastritis, hemorrhoids, indigestion, liver diseases, stomachache and vomiting.
Bombax ceiba	Abdominal pain, colic, constipation, diarrhea, dysentery, emetic, hepatopathy, intestinal spasm, splenopathy, stomach disorders, stomachache and worms.
Catunaregam spinosa	Abdominal spasm, anthelmintic, colic, diarrhea, dysentery, gastritis, indigestion, peptic ulcer and stomachache.
Chenopodium album	Anthelmintic, constipation, digestive disorders, dysentery, dyspepsia, gastritis, hepatic disorders, indigestion, intestinal worms, laxative, peptic ulcer, piles, spleen enlargement and stomach trouble.
Cinnamomum tamala	Appetizer, astringent, colic pain, diarrhea, gastritis, hepatopathy, intestinal disorder, nausea, splenopathy, stomachache and vomiting.
Citrus limon	Carminative, colic, constipation, digestive, dysentery, dyspepsia, intestinal worms, laxative, stomachache and vomiting.
Citrus medica	Appetizer, colic, constipation, diarrhea, digestive, dysentery, dyspepsia, indigestion, laxative, piles and vomiting.
Curculigo orchioides	Cholera, diarrhea, digestive, jaundice, peptic ulcer, piles and stomachache.
Euphorbia royleana	Anthelmintic, appetizer, constipation, diarrhea, dysentery, gastric troubles, indigestion and stomach disorders.
Juniperus indica	Abdominal pain, anthelmintic, appetizer, carminative, constipation, diarrhea, indigestion, laxative, piles and stomachache.
Lagenaria siceraria	Diarrhea, dysentery, indigestion, jaundice, purgative, stomach acidity and ulcer.
Mangifera indica	Abdominal pain, appetizer, biliousness, constipation, diarrhea, dysentery, flatulence, gastritis, gastropathy, hemorrhages, intestinal spasm, jaundice, laxative, peptic ulcer, pharyngopathy, roundworms, stomach disorders, stomach worms and stomachache.
Myristica fragrans	Carminative, colic, diarrhea, digestive, dyspepsia, hepatopathy, stomachache and vomiting.
Nardostachys grandiflora	Anthelmintic, carminative, colic, constipation, diarrhea, digestive, dysentery, dyspepsia, food poisoning, gastritis, indigestion, intestinal parasites, laxative, liver problems and stomach disorders.
Neopicrorhiza scrophulariiflora	Appetizer, bile disorders, gastritis, intestinal pain, intestinal worms, jaundice, liver disorders, purgative and stomachache.
Oroxylum indicum	Appetizer, digestive, dyspepsia, carminative, colic, constipation, diarrhea, dysentery and stomachache.
Oxalis corniculata	Appetizer, biliousness, constipation, diarrhea, digestive, dysentery, dyspepsia, hemorrhoids, indigestion, liver disorders, peptic ulcer, piles, stomach disorders, stomachache and vomiting.
Phyllanthus emblica	Acidity, anthelmintic, colic, constipation, diarrhea, dysentery, dyspepsia, gastric trouble, intestinal spasm, jaundice, laxative, stomachache, stomatitis and vomiting.
Piper longum	Cholagogue, colic, digestive, dyspepsia, indigestion, laxative, piles, splenopathy, stomachache and vomiting.
Psidium guajava	Abdominal pain, anthelmintic, astringent, cholera, colic, constipation, diarrhea and dysentery.
Rubia manjith	Flatulence, gastritis, intestinal spasm, laxative, piles, stomach worms and vomiting.
Terminalia bellirica	Appetizer, biliousness, constipation, diarrhea, digestive, dysentery, dyspepsia, gastritis, gastrointestinal diseases, indigestion, laxative, stomach disorders, stomachache and vomiting.
Terminalia chebula	Carminative, constipation, diarrhea, digestive, dysentery, gastropathy, indigestion, jaundice, laxative, purgative, splenopathy, stomach disorders, stomachache, stomatitis and vomiting.
Thymus linearis	Anthelmintic, appetizer, diarrhea, digestive, gastritis, indigestion, laxative, liver disorders, spleen problems and stomachache.
Trachyspermum ammi	Carminative, cholera, colic, diarrhea, dyspepsia, gastritis, indigestion, intestinal worms and stomachache.
Valeriana jatamansi	Anthelmintic, carminative, cholera, colic, diarrhea, dysentery, gastrospasms, hepato-tonic, indigestion, laxative, splenopathy and stomachache.
Zanthoxylum armatum	Abdominal pain, anthelmintic, appetizer, carminative, cholera, constipation, diarrhea, dysentery, dyspepsia, flatulence, gastritis, indigestion, liver problems, stomach disorders and stomachache.
Zizyphus mauritiana	Abdominal pain, appetizer, constipation, diarrhea, dysentery, dyspepsia, indigestion, laxative, peptic ulcer, stomach disorders and vomiting.

with no phytochemical studies were *Chenopodium album*, *Citrus medica*, and *Rubia manjith*. In-vivo experiments ($n=40$) were more frequent than in-vitro (24). Stomachache was treated by the highest number of species (32), followed by diarrhea (30). In terms of preparation, decoction was the most common form (20 species), followed by paste or powder (16).

3.5. Conservation status

Of all the medicinal plant species used to treat gastrointestinal disorders, 102 species were included in various conservation categories. Forty eight plant species were highly traded (GoN/MoFSC, 1995, 2006; ANSAB, 2013), 42 species were in CAMP threat categories, and 37 in IUCN threat categories. *Nardostachys grandiflora*, *Neopicrorhiza scrophulariiflora*, *Rauvolfia serpentina* and *Taxus wallichiana* were the most threatened species. *Berberis mucrifolia*, *Corydalis megacalyx*, *Delphinium himalayai*, *Euphorbia longifolia* and *Heracleum lallii* were endemic to Nepal. Sixteen orchid species were protected under CITES Appendices II and III (Electronic Appendix 1).

4. Discussion

Medicinal plants are important in primary health care systems in Nepal and thus have been widely studied. However, studies on specific disease types are still lacking except for a few on anthelmintic (Bhattarai, 1992), diarrhea and dysentery (Bhattarai, 1993), gastrointestinal disorders (Thapa et al., 2013) and gynecological treatments (Bhattarai, 1994). Here, we reviewed the literature and documented plant species used in Nepal to treat 20 different disorders related to the digestive system. We focused on gastrointestinal disorders because many people die each year in Nepal due to gastrointestinal related diseases such as diarrhea, dysentery and cholera (Bhandari et al., 2009). The prevalence of these gastrointestinal ailments is likely due to malnutrition, poor hygiene, and lack of clean drinking water, as is the case in India (Dey and De, 2012). Notwithstanding the importance of addressing the public health issues at the root of gastrointestinal disorders, it is as crucial to improve our understanding of how these ailments can be treated. Medicinal plants are part of the solution.

4.1. Diversity, uses, preparation modes

The most common families used to treat gastrointestinal disorders in Nepal were Fabaceae, Asteraceae, Lamiaceae, Rosaceae, and Ranunculaceae. This is in agreement with ethnobotanical studies from Africa, New Zealand and Ecuador (Bennett and Husby, 2008; Saslis-Lagoudakis et al., 2011). A review of medicinal plants used by indigenous people of the Canadian boreal forest also found Asteracea, Rosaceae and Ranunculaceae to be highly used to treat gastrointestinal disorders, along with Liliaceae, Ericaceae, Betulaceae, Caprifoliaceae, and Salicaceae (Uprety et al., 2012a). An ethnobotanical review of the Mapuche medicinal flora of South America (Argentina and Chile) showed that Asteraceae, Rosaceae, Solanaceae, Apiaceae and Fabaceae were frequently used in gastrointestinal problems (Molares and Ladio, 2009).

When using randomization tests to detect which plant families were more commonly used to treat gastrointestinal disorders than expected from their frequency in the total Nepali flora, the Fabaceae, Amaranthaceae, Euphorbiaceae, Anacardiaceae and Lamiaceae families stood out. The comparison between the families used most frequently and the families used more often than expected suggests that Fabaceae and Lamiaceae are not only very common, but host a disproportionately high number of species used against gastrointestinal disorders. In contrast, Asteraceae, Rosaceae and Ranunculaceae are commonly represented among medicinal plants simply because they are common in the Nepali flora. In addition, species from the Asteraceae family are less commonly used against gastrointestinal disorders than would be expected from their representation in the medicinal flora of Nepal. This indicates they are important medicinal plants, but most often used to treat other ailment types. The randomization test we performed highlighted the relative importance of some botanical families in the treatment of a particular type of ailment. Previous studies were conducted in Italy (Weckerle et al., 2012) and in North America (Moerman and Estabrook, 2003), showing that some families were used much more often than would have been expected considering their importance in the local flora. Unfortunately, the randomization test we used is a new addition to the ethnobotanical methodology, and it was thus impossible for us to compare our results with those from other studies. We suggest that the distinction between absolute and relative use frequency is important and that future studies should attempt to perform similar tests. Pharmacological and phytochemical studies should in fact primarily focus on the families hosting more medicinal species than would be expected, as these families show the highest potential.

Underground parts (bulbs, roots, rhizomes, tubers), and fruits and seeds were the most frequent parts used to prepare medicinal formulations, corresponding to previous findings from Nepal (Rokaya et al., 2010; Uprety et al., 2010, 2012b) and elsewhere (Srithi et al., 2009; Kamatenesi et al., 2011; Semenya and Maroyi, 2012). This use pattern is possibly due to higher amounts of bioactive compounds being present in underground parts (Srithi et al., 2009), as well as in seeds or fruits.

4.2. Efficacy of medicinal plants

We found pharmacological and phytochemical studies for 15.87% and 14.27% of the reported plant species, respectively, as was reported in previous studies (Uprety et al., 2010; Luitel et al., 2014). As there is a large number of species used against different gastrointestinal diseases, detailed phytochemical and pharmacological studies of untested species could be carried out to complement traditional knowledge, as was already done for *Aegle marmelos* (Baliga et al., 2011), *Asparagus racemosus* (Alok et al., 2013), *Momordica charantia* (Grover and Yadav, 2004) and *Rheum australe* (Rokaya et al., 2012c).

Chemicals like tannins help inhibit gastric secretions, whereas ellagic acid reduces stress and prevents gastric lesions, especially duodenal ulcers (Murakami et al., 1991), and also relieves diarrhea and dysentery (Heinrich et al. 1992; Pengelly, 2004). Many types of glycosides combined with vitamins (polyphenolic glycosides, flavonoids), alkaloid glycosides, glycosides in the group of antibiotics, glycopeptides, cardiac glycosides, steroids, terpenoid glycosides, etc. (Kren and Martínková, 2001) can be broken down by hydrolysis through the action of enzymes or acids. They are non-toxic, therapeutically beneficial, and exhibit expectorant, sedative, and digestive properties (Pengelly, 2004). Sugars help reduce the fecal volume and rehydrate the patient (Molla et al., 1985). Although it has been pointed out that many secondary metabolites are useful to treat different gastrointestinal diseases, the physiological mechanisms explaining their efficacy are not fully understood.

4.3. Implications for primary health care, bio-prospecting and drug development

Even though many plant species are used in gastrointestinal disorders in Nepal, many people are still dying each year in suburban and rural areas due to diarrhea, dysentery, and cholera. There could be several reasons behind this. First, most plants that are effective in the treatment of gastrointestinal disorders are not necessarily available everywhere and all people do not have specialized knowledge on the required herbal formulations to be used against different disorders due to gaps in knowledge sharing within different communities (Manandhar, 2002; Rokaya et al., 2012b). It was in fact reported that medicinal plants and associated herbal knowledge is not uniformly distributed across the country (Rokaya et al., 2012b). The second, probably most convincing explanation could be related to poverty, low sanitation standards and lack of effective communication (low schooling, lack of health workers, no guidelines available) in many rural areas. Due to this, diseases tend to spread fast and herbal medicines do not allow prompt reaction. Thirdly, due to rapid advancement in modern medicine, more people are attracted to allopathic remedies that cure faster and thus traditional knowledge on plant use—mostly transmitted orally—is dwindling (Shrestha and Dhillion, 2003; Ghimire and Bastakoti, 2009; Bhattarai et al., 2010; Poudel et al., 2013). This is contrary to the western trend toward increased interest for medicinal plants (Jordan et al., 2010).

Our study shows potential for institutionalization of medicinal plants as an alternative and complementary medical system. There are some efforts in promoting the use of herbal medicine from government- and community-based organizations, but primary healthcare remains deficient in remote rural areas. The Ayurvedic Health Care Centers and the traditional *Amchi* (herbalists in mountain regions who follow the Tibetan philosophy) medical systems are the only institutionalized alternative and complementary health care systems in Nepal. The use of herbal medicines should be promoted at the local and national levels, especially in regions where access to allopathic medicines is limited, as medicinal plants are cheaper and associated with less health hazards.

Herbal practitioners are mostly elders. Due to globalization and its influence on cultural settings in several areas including the Himalaya, knowledge transfer to new generations is not as efficient as it used to be (Bhattarai et al., 2006; Luitel et al., 2014), leading to depletion of traditional knowledge at an unprecedented scale. Therefore, to preserve traditional medicinal knowledge, the importance of herbal practitioners and their role in primary health care systems should be recognized at the national level. Capacity building of herbal practitioners and education of new generations will have substantial impact on the long-term sustainability of herbal knowledge.

Less than 16% of the plants reported in this study have been tested for biochemical efficacy, leaving room for bio-prospecting and testing.

The 35 plant species that are used to treat the highest number of gastrointestinal disorders could be of interest from a pharmacological perspective. Traditional uses of medicinal plants also need to be evaluated in terms of toxicity and for their potential side effects and interactions before integrating into modern health care systems. Commercial exploitation of medicinal plants should, however, make sure to safeguard the intellectual property rights of local people and traditional medicine (Saslis-Lagoudakis et al., 2012) and respect the conservation status of plant species (Hamilton, 2004).

4.4. Conservation status of medicinal plants

Nepal has a high biodiversity due to climatic and topographic variation (Chaudhary, 1998). There are many plant species that are endemic (Shrestha and Joshi, 1996) and have medicinal value (Rokaya et al., 2012a). A large number of medicinal plant species are traded within the country (Tiwari et al., 2004) or exported outside (Edwards, 1996; Olsen and Helles, 1997; Olsen and Bhattarai, 2005). Collection and trade of wild medicinal plants have largely contributed to rural economy in Nepal. Apart from trade and medicinal purposes, several species are used as fodder, timber, firewood, etc. (e.g., *Acacia catechu*, *Bombax ceiba*, *Juniperus* spp., *Mangifera indica*, *Pterocarpus marsupium*, *Taxus* spp.). Multiple uses exert higher demand, leading to increased harvest, and such actions raise threats for some species. Most plant species are collected from the wild in unsustainable manners, also threatening species. Apart from harvesting, different factors such as deforestation, habitat encroachment, overgrazing, wildfires, shifting cultivation, and climate change contribute to species loss (Chaudhary, 1998; Uprety et al., 2011a, 2011b; Kunwar et al., 2013). It is thus important to identify valuable species, precisely map their distribution, document their status, study their life cycle, and formulate guidelines for their conservation and management.

5. Conclusion

In this review, we described the medicinal plants used in Nepal to treat gastrointestinal disorders. Parts used, administration process and doses can be of high value for drug formulation. Commercial exploitation of medicinal plants should make sure to safeguard the intellectual property rights of local people.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.jep.2014.10.014.

References

Aburjai, T., Natsheh, F.M., 2003. Plants used in cosmetics. Phytotherapy Research 17, 987–1000.
Alok, S., Jain, S.K., Verma, A., Kumar, M., Mahor, A., Sabharwal, M., 2013. Plant profile, phytochemistry and pharmacology of *Asparagus racemosus* (Shatavari): a review. Asian Pacific Journal of Tropical Disease 3, 242–251.
Anh, D.D., Lopez, A.L., Thiem, V.D., Grahek, S.L., Duong, T.N., Park, J.K., Kwon, H.J., Favorov, M., Hien, N.T., Clemens, J.D., 2011. Use of oral cholera caccines in an outbreak in Vietnam: a case control study. PLoS Neglected Tropical Diseases 5, e1006.
ANSAB, 2013. The Asia Network for Sustainable Agriculture and Bioresources [WWW Document]. URL ⟨http://www.ansab.org⟩ (accessed 06.04.13.).
Baliga, M.S., Bhat, H.P., Joseph, N., Fazal, F., 2011. Phytochemistry and medicinal uses of the bael fruit (*Aegle marmelos* Correa): a concise review. Food Research International 44, 1768–1775.
Baral, S.R., Kurmi, P.P., 2006. A Compendium of Medicinal Plants in Nepal. Rachana Sharma, Kathmandu, Nepal.
Bartels, S.A., Greenough, P.G., Tamar, M., VanRooyen, M.J., 2010. Investigation of a cholera outbreak in Ethiopia's Oromiya Region. Disaster Medicine and Public Health Preparedness 4, 312.
Bennett, B.C., Husby, C.E., 2008. Pattern of medicinal plant use: an examination of the Ecuadorian Shuar medicinal flora using contingency table and binomial analyses. Journal of Ethnopharmacology 116, 422–430.
Bernal, J., Mendiola, J.A., Ibáñez, E., Cifuentes, A., 2011. Advanced analysis of nutraceuticals. Journal of Pharmaceutical and Biomedical Analysis 55, 758–774.
Bhandari, G.P., Dixit, S.M., Ghimire, U., Maskey, M.K., 2009. Outbreak investigation of diarrheal diseases in Jajarkot. Journal of Nepal Health Research Council 7, 66–68.
Bhattarai, N.K., 1992. Folk anthelmintic drugs of central Nepal. Pharmaceutical Biology 30, 145–150.
Bhattarai, N.K., 1993. Folk herbal remedies for diarrhea and dysentery in central Nepal. Fitoterapia 64, 243–250.
Bhattarai, N.K., 1994. Folk herbal remedies for gynaecological complaints in central Nepal. Pharmaceutical Biology 32, 13–26.
Bhattarai, S., Chaudhary, R.P., Quave, C.L., Taylor, R.S., 2010. The use of medicinal plants in the trans-himalayan arid zone of Mustang district, Nepal. Journal of Ethnobiology and Ethnomedicine 6, 14.
Bhattarai, S., Chaudhary, R.P., Taylor, R.S., 2006. Ethnomedicinal plants used by the people of Manang district, central Nepal. Journal of Ethnobiology and Ethnomedicine 2, 41.
Blumenthal, M., 2002. Herb sales down in mainstream market, up in natural food stores. HerbalGram 55, 60.
CAMP, 2001. Conservation Assessment and Management Prioritization Report. International Development Research Centre (IDRC), Canada/Ministry of Forest and Soil Conservation, HMG, Nepal.
Chaudhary, R.P., 1998. Biodiversity in Nepal: Status and Conservation. Tecpress Books, Bangkok, Thailand.
CITES, 2013. Convention on International Trade in Endangered Species of Wild Fauna and Flora [WWW Document]. URL ⟨http://cites.org/⟩ (accessed 13.06.13.).
Coburn, B., 1984. Some native medicinal plants of the western Gurung. Kailash 11, 55–88.
Cook, F.E.M., 1995. Economic Botany Data Collection Standard. Royal Botanic Gardens, Kew.
Dey, A., De, J.N., 2012. Ethnobotanical survey of Purulia district, West Bengal, India for medicinal plants used against gastrointestinal disorders. Journal of Ethnopharmacology 143, 68–80.
Douwes, E., Crouch, N.R., Edwards, T.J., Mulholland, D.A., 2008. Regression analyses of southern African ethnomedicinal plants: informing the targeted selection of bioprospecting and pharmacological screening subjects. Journal of Ethnopharmacology 119, 356–364.
Edwards, D.M., 1996. The trade in non-timber forest products from Nepal. Mountain Research and Development 16, 383–394.
Espín, J.C., García-Conesa, M.T., Tomás-Barberán, F.A., 2007. Nutraceuticals: facts and fiction. Phytochemistry 68, 2986–3008.
Fisher, D., 2009. Cholera in Zimbabwe. Annals of the Academy of Medicine, Singapore 38, 82.
Gaire, B.P., Subedi, L., 2011. Medicinal plant diversity and their pharmacological aspects of Nepal Himalayas. Pharmacognosy Journal 2, 6–17.
Ghimire, K., Bastakoti, R.R., 2009. Ethnomedicinal knowledge and healthcare practices among the Tharus of Nawalparasi district in central Nepal. Forest Ecology and Management 257, 2066–2072.
GoN/MoFSC, 1995. Forest Act, 1993 and Forest Regulation, 1995. Ministry of Forests and Soil Conservation, Nepal.
GoN/MoFSC, 2006. Nepalko Antarik Bikaskalagi Prathamikata Prapta Jadibutiharu. Ministry of Forests and Soil Conservation, Nepal.
Griggs, J., Manandhar, N.P., Towers, G.H., Taylor, R.S., 2001. The effects of storage on the biological activity of medicinal plants from Nepal. Journal of Ethnopharmacology 77, 247–252.
Grover, J., Yadav, S., 2004. Pharmacological actions and potential uses of *Momordica charantia*: a review. Journal of Ethnopharmacology 93, 123–132.
Hamilton, A.C., 2004. Medicinal plants, conservation and livelihoods. Biodiversity and Conservation 13, 1477–1517.
Heinrich, M., Rimpler, H., Barrera, N.A., 1992. Indigenous phytotherapy of gastrointestinal disorders in a lowland Mixe community (Oaxaca, Mexico): ethnopharmacologic evaluation. Journal of Ethnopharmacology 36, 63–80.
IUCN, 2013. IUCN redlist [WWW Document]. The IUCN Red list of Threatened Species. URL ⟨http://www.iucnredlist.org⟩ (accessed 06.04.13.).
Jordan, S.A., Cunningham, D.G., Marles, R.J., 2010. Assessment of herbal medicinal products: challenges, and opportunities to increase the knowledge base for safety assessment. Toxicology and Applied Pharmacology 243, 198–216.
Joshi, A.R., Joshi, K., 2005. Ethnobotany and Conservation of Plant Diversity in Nepal: Status, Bibliography and Agenda for Sustainable Management, first edition RubRick, Kathmandu, Nepal.
Kamatenesi, M.M., Acipa, A., Oryem-Origa, H., 2011. Medicinal plants of Otwal and Ngai Sub Counties in Oyam district, Northern Uganda. Journal of Ethnobiology and Ethnomedicine 7, 7.

Karki, A., Tiwari, B.R., 2007. Prevalence of acute diarrhoea in Kathmandu valley. Journal of Nepal Medical Association 46, 175–179.
Kren, V., Martínková, L., 2001. Glycosides in medicine: the role of glycosidic residue in biological activity. Current Medicinal Chemistry 8, 1303–1328.
Kunwar, R.M., Bussmann, R.W., 2008. Ethnobotany in the Nepal Himalaya. Journal of Ethnobiology and Ethnomedicine 4, 24.
Kunwar, R.M., Mahat, L., Acharya, R.P., Bussmann, R.W., 2013. Medicinal plants, traditional medicine, markets and management in far-west Nepal. Journal of Ethnobiology and Ethnomedicine 9, 24.
Kunwar, R.M., Uprety, Y., Burlakoti, C., Chowdhary, C.L., Bussmann, R.W., 2009. Indigenous use and ethnopharmacology of medicinal plants in far-west Nepal. Ethnobotany Research & Applications 7, 005–028.
Lama, Y.C., Ghimire, S.K., Aumeeruddy-Thomas, Y., 2001. Medicinal Plants of Dolpo: Amchis' Knowledge and Conservation. Worldwide Fund for Nature Conservation (WWF) Nepal, Kathmandu, Nepal.
Lepš, J., Šmilauer, P., 2003. Multivariate Analysis of Ecological Data Using CANOCO. Cambridge University Press.
Luitel, D.R., Rokaya, M.B., Timsina, B., Münzbergová, Z., 2014. Medicinal plants used by the Tamang community in the Makawanpur district of central Nepal. Journal of Ethnobiology and Ethnomedicine 10, 5.
Madikizela, B., Ndhlala, A.R., Finnie, J.F., Van Staden, J., 2012. Ethnopharmacological study of plants from Pondoland used against diarrhoea. Journal of Ethnopharmacology 141, 61–71.
Manandhar, N.P., 2002. Plants and People of Nepal. Timber Press, Portland, OR, USA.
Mathabe, M.C., Nikolova, R.V., Lall, N., Nyazema, N.Z., 2006. Antibacterial activities of medicinal plants used for the treatment of diarrhoea in Limpopo Province, South Africa. Journal of Ethnopharmacology 105, 286–293.
MATLAB 5.3, 1999. MATLAB®—The Language of Technical Computing Version 5.3.1.29215aR11.1. The MathWorks Inc., USA.
Moerman, D.E., Estabrook, G.F., 2003. Native Americans' choice of species for medicinal use is dependent on plant family: confirmation with meta-significance analysis. Journal of Ethnopharmacology 87, 51–59.
Molares, S., Ladio, A., 2009. Ethnobotanical review of the Mapuche medicinal flora: use patterns on a regional scale. Journal of Ethnopharmacology 122, 251–260.
Molla, A.M., Greenough, W.G., Molla, M., Khatun, M., Majid, N., Rohde, J., 1985. Rice water is not rice cereal oral rehydration solution. Lancet II, 40.
Mukherjee, P.K., Wahile, A., 2006. Integrated approaches towards drug development from Ayurveda and other Indian system of medicines. Journal of Ethnopharmacology 103, 25–35.
Murakami, S., Isobe, Y., Kijima, H., Nagai, H., Muramatu, M., Otomo, S., 1991. Inhibition of gastric H+, K(+)-ATPase and acid secretion by ellagic acid. Planta Medica 57, 305–308.
Neamsuvan, O., Tuwaemaengae, T., Bensulong, F., Asae, A., Mosamae, K., 2012. A survey of folk remedies for gastrointestinal tract diseases from Thailand's three southern border provinces. Journal of Ethnopharmacology 144, 11–21.
Newman, D.J., Cragg, G.M., 2007. Natural products as sources of new drugs over the last 25 Years. Journal of Natural Products 70, 461–477.
Olsen, C.S., Bhattarai, N., 2005. A typology of economic agents in the Himalayan plant trade. Mountain Research and Development 25, 37–43.
Olsen, C.S., Helles, F., 1997. Medicinal plants, markets, and margins in the Nepal Himalaya: trouble in paradise. Mountain Research and Development 17, 363–374.
Panthi, M.P., Chaudhary, R.P., 2006. Antibacterial activity of some selected folklore medicinal plants from west Nepal. Scientific World 4, 16–21.
Pawlowski, S.W., Warren, C.A., Guerrant, R., 2009. Diagnosis and treatment of acute or persistent diarrhea. Gastroenterology 136, 1874–1886.
Pengelly, A., 2004. Constituents of Medicinal plants: An Introduction to the Chemistry and Therapeutics of Herbal Medicine. Allen & Unwin, Australia.
Pohle, P., 1990. Useful Plants of Manang District: A Contribution to the Ethnobotany of the Nepal-Himalaya. Franz Steiner Verlag Wiesbaden GMBH, Stuttgart.
Polunin, O., Stainton, A., 1984. Flowers of the Himalaya. Oxford University Press, New Delhi, India.
Poudel, R.C., Gao, L.-M., Möller, M., Baral, S.R., Uprety, Y., Liu, J., Li, D.-Z., 2013. Yews (Taxus) along the Hindu Kush-Himalayan region: exploring the ethnopharmacological relevance among communities of Mongol and Caucasian origins. Journal of Ethnopharmacology 147, 190–203.
Press, J.R., Shrestha, K.K., Sutton, D.A., 2000. Annotated Checklist of the Flowering Plants of Nepal. Natural History Museum, London and Central Department of Botany, Tribhuvan University, Kathmandu.
Rajbhandari, K.R., 2001. Ethnobotany of Nepal. Ethnobotanical Society of Nepal, Kathmandu, Nepal.
Rajbhandari, M., Mentel, R., Jha, P.K., Chaudhary, R.P., Bhattarai, S., Gewali, M.B., Karmacharya, N., Hipper, M., Lindequist, U., 2009. Antiviral activity of some plants used in Nepalese traditional medicine. Evidence-Based Complementary and Alternative Medicine 6, 517–522.
Rokaya, M.B., Maršík, P., Münzbergová, Z., 2012a. Active constituents in *Rheum acuminatum* and *Rheum australe* (Polygonaceae) roots: a variation between cultivated and naturally growing plants. Biochemical Systematics and Ecology 41, 83–90.
Rokaya, M.B., Münzbergová, Z., Shrestha, M.R., Timsina, B., 2012b. Distribution patterns of medicinal plants along an elevational gradient in central Himalaya, Nepal. Journal of Mountain Science 9, 201–213.
Rokaya, M.B., Münzbergová, Z., Timsina, B., 2010. Ethnobotanical study of medicinal plants from the Humla district of western Nepal. Journal of Ethnopharmacology 130, 485–504.
Rokaya, M.B., Münzbergová, Z., Timsina, B., Bhattarai, K.R., 2012c. *Rheum australe* D. Don: a review of its botany, ethnobotany, phytochemistry and pharmacology. Journal of Ethnopharmacology 141, 761–774.
Ryan, E.T., 2011. The cholera pandemic, still with us after half a century: time to rethink. PLoS Neglected Tropical Diseases 5, e1003.
Sarkar, R., Prabhakar, A.T., Manickam, S., Selvapandian, D., Raghava, M.V., Kang, G., Balraj, V., 2007. Epidemiological investigation of an outbreak of acute diarrhoeal disease using geographic information systems. Transactions of the Royal Society of Tropical Medicine and Hygiene 101, 587–593.
Saslis-Lagoudakis, C.H., Savolainen, V., Williamson, E.M., Forest, F., Wagstaff, S.J., Baral, S. R., Watson, M.F., Pendry, C.A., Hawkins, J.A., 2012. Phylogenies reveal predictive power of traditional medicine in bioprospecting. Proceedings of the National Academy of Sciences of the United States of America 109, 15835–15840.
Saslis-Lagoudakis, C.H., Williamson, E.M., Savolainen, V., Hawkins, J.A., 2011. Cross-cultural comparison of three medicinal floras and implications for bioprospecting strategies. Journal of Ethnopharmacology 135, 476–487.
Semenya, S.S., Maroyi, A., 2012. Medicinal plants used by the Bapedi traditional healers to treat diarrhoea in the Limpopo Province, South Africa. Journal of Ethnopharmacology 144, 395–401.
Shrestha, K.K., Tiwari, N.N., Rajbhandari, S., Poudel, R.C., Uprety, Y., 2004. Ethnobotany in Nepal: Review and Perspectives. WWF Nepal Program, Kathmandu, Nepal.
Shrestha, P.M., Dhillion, S.S., 2003. Medicinal plant diversity and use in the highlands of Dolakha district, Nepal. Journal of Ethnopharmacology 86, 81–96.
Shrestha, T.B., Joshi, R.M., 1996. Rare, Endemic and Endangered Plants of Nepal. WWF Nepal, Kathmandu, Nepal.
Soejarto, D.D., Fong, H.H.S., Tan, G.T., Zhang, H.J., Ma, C.Y., Franzblau, S.G., Gyllenhaal, C., Riley, M.C., Kadushin, M.R., Pezzuto, J.M., Xuan, L.T., Hiep, N.T., Hung, N.V., Vu, B.M., Loc, P.K., Dac, L.X., Binh, L.T., Chien, N.Q., Hai, N.V., Bich, T.Q., Cuong, N.M., Southavong, B., Sydara, K., Bouamanivong, S., Ly, H.M., Thuy, T.V., Rose, W.C., Dietzman, G.R., 2005. Ethnobotany/ethnopharmacology and mass bioprospecting: Issues on intellectual property and benefit-sharing. Journal of Ethnopharmacology 100, 15–22.
Srithi, K., Balslev, H., Wangpakapattanawong, P., Srisanga, P., Trisonthi, C., 2009. Medicinal plant knowledge and its erosion among the Mien (Yao) in northern Thailand. Journal of Ethnopharmacology 123, 335–342.
Stainton, A., 1988. Flowers of the Himalaya: A Supplement. Oxford University Press, New Delhi, India.
Storrs, A., Storrs, J., 1998. Trees and Shrubs of Nepal and the Himalayas. Books Faith India, New Delhi, India.
Street, R.A., Prinsloo, G., 2013. Commercially important medicinal plants of South Africa: a review. Journal of Chemistry 2013, 1–16.
ter Braak, C.J.F., Smilauer, P., 2012. Canoco Reference Manual and User's Guide: Software for Ordination, Canoco 5. Biometris, Plant Research International, The Netherlands and Czech Republic.
Thapa, L.B., Dhakal, T.M., Chaudhary, R., Thapa, H., 2013. Medicinal plants used by Raji ethnic tribe of Nepal in treatment of gastrointestinal disorders. Our Nature 11, 177–186.
Tiwari, N.N., Poudel, R.C., Uprety, Y., 2004. Study on Domestic Market of Medicinal and Aromatic Plants (MAPs) in Kathmandu Valley. Winrock International, Kathmandu, Nepal.
Tuite, A.R., Tien, J., Eisenberg, M., Earn, D.J.D., Ma, J., Fisman, D.N., 2011. Cholera epidemic in Haiti, 2010: using a transmission model to explain spatial spread of disease and identify optimal control interventions. Annals of Internal Medicine 154, 593–601.
Uprety, Y., Asselin, H., Boon, E.K., Yadav, S., Shrestha, K.K., 2010. Indigenous use and bio-efficacy of medicinal plants in the Rasuwa district, central Nepal. Journal of Ethnobiology and Ethnomedicine 6, 3.
Uprety, Y., Asselin, H., Dhakal, A., Julien, N., 2012a. Traditional use of medicinal plants in the boreal forest of Canada: review and perspectives. Journal of Ethnobiology and Ethnomedicine 8, 7.
Uprety, Y., Poudel, R.C., Asselin, H., Boon, E., 2011a. Plant biodiversity and ethnobotany inside the projected impact area of the Upper Seti Hydropower Project, Western Nepal. Environment, Development and Sustainability 13, 463–492.
Uprety, Y., Poudel, R.C., Asselin, H., Boon, E.K., Shrestha, K.K., 2011b. Stakeholder perspectives on use, trade, and conservation of medicinal plants in the Rasuwa district of central Nepal. Journal of Mountain Science 8, 75–86.
Uprety, Y., Poudel, R.C., Shrestha, K.K., Rajbhandary, S., Tiwari, N.N., Shrestha, U.B., Asselin, H., 2012b. Diversity of use and local knowledge of wild edible plant resources in Nepal. Journal of Ethnobiology and Ethnomedicine 8, 16.
Weckerle, C.S., Cabras, S., Castellanos, M.E., Leonti, M., 2012. An imprecise probability approach for the detection of over and underused taxonomic groups with the Campania (Italy) and the Sierra Popoluca (Mexico) medicinal flora. Journal of Ethnopharmacology 142, 259–264.
WHO, 2008. Traditional Medicine Fact Sheet 134 [WWW Document]. World Health Organization. URL ⟨http://www.who.int/mediacentre/factsheets/fs134/en/⟩ (accessed 26.02.13.).