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Phytochemical Properties and Pharmacological Role of Plants: Secondary Metabolites

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Over the past decades, there has been increasing attention to the study of medicinal plants that contain many phytochemicals beneficial for human health. A number of secondary metabolites derived from various plants have been used as drug components to treat several human disorders since ancient times. The traditional therapeutic applications of secondary metabolites have been reported in the whole world. Numerous bioactive phytochemicals constituents have been identified and isolated using many advanced techniques. These bioactive phytochemicals are responsible for many pharmacological activities such as anti-inflammation, anti-cancer, anti-allergic, and antimicrobial infection. These secondary metabolites are not only beneficial for human health but also protect plants themselves from biotic and abiotic stress. These secondary metabolites are classified into many subclasses like terpenoids, alkaloids and phenolics. Each class of secondary metabolites has its pharmacological activities, which is required to be studied thoroughly for better use in pharmaceuticals, cosmetics, food, and other industries. Therefore, this review paper represents many medicinal plants that contain bioactive secondary metabolites and show pharmacological activities, which provides an opportunity to utilize them for improvement of human health and discover new herbal medicines.

Keywords: Secondary metabolites, Bioactive, Pharmaceutical, Terpenoids, Alkaloids, Phenolics.

Today's lifestyle is a leading cause to many human diseases. Allopathic medicines often work effectively against the disease but may show extreme side effects in certain cases. Commonly manifested side effects of allopathic medicines are face swelling, rashes on the body, itching, headache, inflammation, and drug resistance. A safer alternative to treat diseases is herbal or plant derived medicines that have been used since the ancient period (Kabera *et.al* 2014). India and China provide the best example of the early use of medicinal plants. Both countries enlist countless plant-derived medicines (Tang *et.al* 1992). The diversity of medicinal plants depends on many factors such as climate, altitude, seasonal fluctuations etc. While many plants are perennial and live for many years contributing as a consistent source of medicinal compounds, other plants have shorter life span ranging from seasonal to annual or biennial. There is a huge variety of seasonal plants that show medicinal properties, some plants grow in summer, some in winters, and some plants

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occur only in the spring season. Some examples of medicinal plants that grow in different seasons are *Achillea filipendulina, Santolina chamecyparissus,* and *Mentha longifolia* grows in summer, *Cistus monspeliensi, Ocimum gratissimum* grows in the spring season (Soni *et.al* 2015).

The versatile and vast pharmacological effects of medicinal plants are completely dependent on their phytochemical constituents. Various phytochemicals of plants have been isolated for drug discovery and development. Modern analytical techniques such as electrophoresis, chromatography, enzymology, and isotope techniques have been used to characterize phytochemicals, elucidate their structural formulas and decipher their biosynthetic pathways (Hussein *et.al* 2018, Okada *et.al* 2010). To explore the therapeutic use of plants, it is pertinent to have deep understanding of phytochemistry and have detailed knowledge of phytochemical composition of plant extracts which further can be used to develop different medicines.

Generally, the phytochemicals are divided into two categories i.e. primary and secondary metabolites based on their role in different metabolic processes. Primary metabolites are involved in primary processes such as respiration, growth, cell division, photosynthesis and food storage. The biomolecules such as carbohydrates, amino acids and lipids are categorized as primary metabolites as they are fundamental reactants and intermediates in carbon metabolism, nitrogen metabolism and associated pathways (Seigler *et.al* 1995). On the other hand, secondary metabolites are derived from primary metabolites in a very small amount, usually at a certain growth stage or to serve a specific function. Secondary metabolites provide the ability to defend against biotic and abiotic stress in plants. The mechanism of defence in plants varies according to the specific requirements of plants and is affected by physiological conditions, climate variations and environmental factors (Ballhorn *et.al* 2009, Blank *et.al* 2012).

Plant secondary metabolites are broadly divided into three categories: Terpenoids, Alkaloids, and Phenolics (Savithramma *et.al* 2011). Each of these classes of secondary metabolites includes a huge array of compounds that have

Table 1. Pharmacological Activities of Secondary Metabolites

Name of secondary metabolites	Pharmacological activities	References
Linalool	Antibacterial, exert an effect on CNS	Taniguchi *et.al* 2014, Zhang *et.al* 1987
Codeine	Antitussive, antidepressant, analgesic, sedative, and hypnotic properties	Smith *et.al* 2006, Vree *et.al* 2000
Morphine	Acute pulmonary edam and reduce the shortness of breath	Takita *et.al* 2000
Quinine	Antipyretic. Antimalarial, analgesic	EI-Tawil *et.al* 2010, Mwita *et.al* 2012
Atropine	Anti-cholinergic, ant myopia, effects competitive antagonist of muscarine acetylcholine receptors	Gu *et.al* 2011
Nicotine	Insecticide, anti-inflammatory, antiherbivore	Melton *et.al* 2006, Rhoades *et.al* 1976
Berberine	Antiviral, antibacterial, anticancer, antidiabetic, and anti-inflammatory	Zha *et.al* 2010, Zhang *et.al* 2010
Gallic acid	antibacterial, antiviral, antifungal, anti-inflammatory, antitumor, ant anaphylactic, antimutagenic, choleretic, and bronchodilator actions and promote muscle relaxation	Harborne *et.al* 1993
Hydroquinone	Antimicrobial and used as antiseptics	Pelczar *et.al* 1988
hydrolyzable tannins	Anti-diarrhoeal, antidotes in poisoning by heavy metals, antiangiogenic, also treat urinary tract infections	Jepson *et.al* 2008
Coumarins	Anti-inflammatory, anticoagulant, anticancer, and anti-Alzheimer's	Xu *et.al* 2015

been found effective to treat different diseases, some of these compounds are- atropine, codeine, morphine, and nicotine, coming under alkaloids; linalool comes under terpenoids, while flavonoids, lignans and proanthocyanidins are categorized as phenolics. In the present review, secondary metabolites are studied thoroughly that include properties of secondary metabolites, biosynthetic pathways of secondary metabolites, structures and classification of secondary metabolites, and their pharmacological activities. Pharmacological activities of some secondary metabolites that have been used to treat various diseases are enlisted in the given table (Table 1).

Description of classes of secondary metabolites

Secondary metabolites can be classified based on their chemical composition. These phytochemicals are divided into three broad categories- Alkaloids, Phenolics and Terpenoids, as already mentioned above. A brief description of each of these categories is given further.

Alkaloids

Alkaloids are nitrogen-containing compounds which are widely distributed among large number of plant families. These compounds can be found in the whole plant or sometimes in a specific part of the plant. It is a highly diverse and large group consisting of more than 1800 alkaloids, all of which are different from each other and have different chemical structures. Alkaloids contain one or more nitrogen groups in their chemical structures. A number of researches have shown potential pharmacological effects and curative properties of alkaloids against many human diseases and disorders. There is a huge list of alkaloids that are used in pharmacological

Table 2. List of plants that contain pharmacologically important alkaloids

S. No.	Name of the plant	Alkaloids	References
1	*Liriodendron tulipifera L.*	Aporphine, liriodenine, lysicamine, lanuginosine	Ziyaev *et.al* 1987
2	*Nitraia schoberi L.*	Schoberine, nitraraine, nitraramine, sibiridine, vasicinone	Tulyaganov and Kozimova 2005
3	*Convolvulus subhirsutus*	Convolvine, convolamine, convolidine, phyllabine, phyllalbine, nortropine, conpropine	Gapparov *et.al* 2007
4	*Convolvulus pseudocanthabrica schrenk*	Convolvine, convolamine, convolvidine, convolicine	Gapparov and Aripova *et.al* 2011
5	*Arundo donax L.*	Deoxyvasicinone, ardine, donine, donaxarine, arundamine	Khuzhaev *et.al* 2004
6	*Crambe kotschyana*	Goitrin and goiridin	Okhunov *et.al* 2011

Table 3. Classification of phenolic compounds with their pharmacological activities

Types of phenolic compounds	Pharmacological activities
Simple phenols	Treat urinary tract infections, antimicrobial, anti-inflammation and used as antiseptic in surgeries
Tannins	Used to convert raw animal hides into leather, anti-diarrhoeal, antidotes in poisoning
Coumarins	Anticoagulant aand anti-Alzheimer
Flavonoids	Antithrombotic, anti-allergic, vasoproptective, inhibit tumour to grow and protect gastric mucosa
Xanthos	Antifungal
Stilbenes	Helps in the production of Estrogen
Lignans	Antimicrobial, antifungal activities

activities. Some of the alkaloids are enlisted in the Table 2 given below (Egamberdieva *et.al* 2017).

Phenolic compounds

Phenolic compounds encompass a large number of phytochemicals consisting of one or more phenol groups. Phenols are responsible for the color, flavor, and taste of many herbs that are used in drinks and food. These secondary metabolites are highly valued for their pharmacological activities. Phenols are also used in many drugs due to their important pharmacological properties such as antioxidant, anti-microbial, anti-inflammatory, anti-cancer etc. Phenols are classified on the basis of their different chemical structures, enlisted in

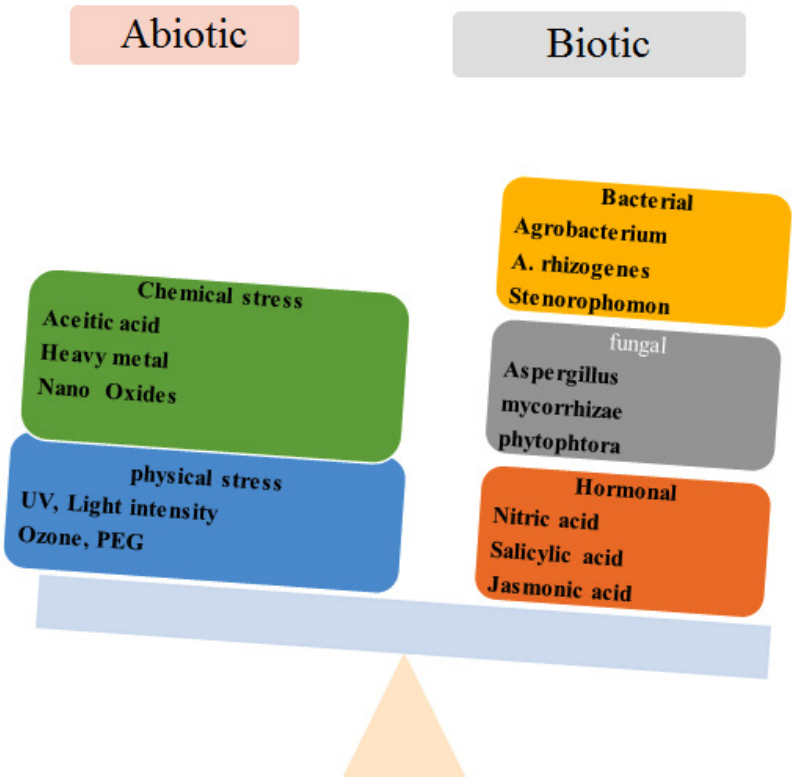


Fig. 1. Representation of plant stresses

Table 4. Classification of terpenes

Name of Terpenes	Name of terpenoids	Location of terpenoids	References
Hemiterpene (C_5)	Isoprenenol Isovalenic acid	Synthesis Essential oils	Eadie *et.al* 2004. Ara *et.al* 2006, Elson *et.al* 1988
Monoterpene (C_{10})	Limonene	Essential oil	Espina *et.al* 2013
Sesquiterpene (C_{15})	ABA (Abscisic acid)		Zhang *et.al* 1987
Diterpene (C_{20})	Gibberellin	Gibberella fujikuroi	Hakoshima *et.al* 2011
Triterpene (C_{30})	Brassinosteroids	Lychins viscaria, Brassica napus	Coelho *et.al* 2013, Krishna *et.al* 2003
Tetraterpene (C_{40})	Carotenoids	Carrot, chloroplast, and chromoplasts of plants	M.M *et.al* 2014

Table 5. Secondary metabolites and their examples

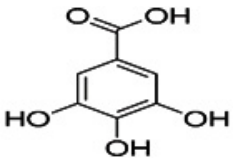
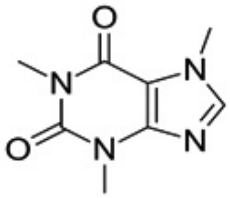
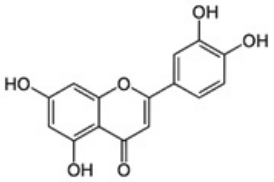
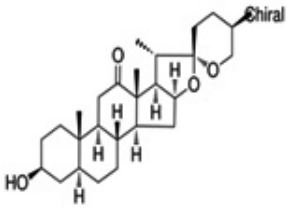
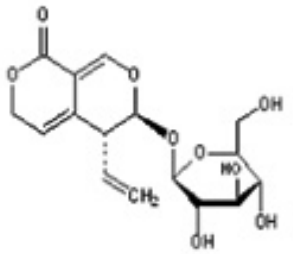
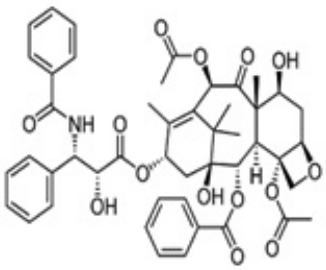
S. No.	Phytochemical name	Chemical structure	Example	Reference
1	Polyphenols		Resveratrol, caffeic acid, gallic acid, quercetin and flavones	Hussein *et.al* 2018
2	Alkaloids		Caffeine, codeine, berberin, morphine	Sarker *et.al* 2007
3	Anthraquinones		Luteolin, rhein, salinos, poramide and salinos	Augustin *et.al* 2005
4	Saponins		Diosgenin and hecogenin	Firn *et.al* 2010
5	Glycosides		Cinnamyl acetate, amygdalin, gentiopicrin, polygalin, and rographolide	Kar *et.al* 2010
6	Terpenes		Carotenoids and steroids, artemisinin, lycopene, lutein, and zeaxanthin	Kar *et.al* 2010

Table 3 given below, along with their respective pharmacological activities (Puneet *et.al* 2013, Montanher *et.al* 2007, Serafini *et.al* 2010).

Terpenes

Terpenes also form a diverse group of plant secondary metabolites that mainly consist of a five-carbon isoprene unit. Terpenes are classified according to the number of isoprene units in the molecule, the classes are summarized in Table 4 (Hoffmann *et.al* 2003).

Some secondary metabolites recognized for their pharmacological activities along with their general chemical structures and examples are enlisted in Table 5.

Properties of phytochemicals and Pharmacological activities of plants

Plants survived on the planet for more than 400 million years. Plants cannot move from one place to another so they have to face lots of biotic and abiotic stress that are represented in Figure 1. Plants neither have any active weapon to attack plant-eating animals or herbivores and microbes, nor do they have any shield to protect themselves from environmental stress. Secondary metabolites serve as the defense system of plants as they protect them from all the biotic and abiotic stresses (Asif 2015). Owing to their bioactivity, secondary metabolites have been historically used not only in Indian medicines (Ayurveda) but also used traditionally in Kampo medicines, European medicines, American, Australian, and traditional medicine system of Africa. There is extensive research that has been carried out in search of novel and safe plant derived medicine. For example, Alorkpa *et.al* 2016 extracted out bioactive compounds from *Carica papaya* leaves and investigated their antimicrobial activity. They identified the presence of many secondary metabolites such as alkaloids, flavonoids, saponins and glycosides and found that the extracts showed antimicrobial activity against human pathogenic bacteria and fungi. Plant derived extracts and compounds have many beneficial uses due to their biochemical, pharmaceutical and therapeutic properties.

Some of the uses and beneficial properties of phytochemicals are enlisted in Table 6 given below

Secondary metabolites work alone or in combination with other compounds/ metabolites to cure diseases. Such combinations can enhance the efficacy of treatment of a disease which have been proven in many studies (Wink *et.al* 2015). Many phytochemicals have shown great success to defeat the dreadful disease like cancers (Seca *et.al* 2018, Raina *et.al* 2014). The medicinal plant *Hypericum perforatum* is used for it anti-depressant, anti-inflammatory, antiviral, anticancer, and antibacterial properties. This plant contains fluoxetine and sertraline that cures depression, and other metabolites like hypericin, hyperforin, flavonoids and xanthones, which further enhance its medicinal value (Shakya *et.al* 2017). Badgujar *et.al* in 2014 studied the use of *Ficus carica* to treat many disorders that are related to the digestive, endocrine, reproductive, and respiratory system. *Ficus carica* belongs to angiosperm genera and consists of more than 800 different species. *Phaleria macrocarpa* belongs to Thymelaeaceae family and has been traditionally used in Malaysia and Indonesia. Many diseases such as rheumatism, high blood pressure, diabetes mellitus, cancer, skin diseases, allergies, stroke, migraine, and hemorrhoids have been treated using this plant (Or *et.al* 2016). *Echinacea purpurea,* a medicinal herb with many secondary metabolites, has been

Table 6. Example of plant molecules that used for human health

Phytochemicals	Properties	References
Menthol, benzyl acetate, linalool, limonene, 2-phenylthel alcohol, vanillin	Flavors	Altemimi *et.al* 2017
Vitamins, Taxol, quinine, minerals, amino-acids, enzymes, morphine, polysaccharides	Health	Fridlender *et.al* 2015
Stevioside, rebaudioside	Sweeteners	Soejarto *et.al* 2019
Vitamins, non-dairy milk, genistein, daidzein, lycopene, genistein, daidzein, resveratrol	food and nutrition	Rahal *et.al* 2014

Table 7. Pharmalogical activities of medicinal plants with their common names

S. No.	Name of plant species	Common name of plant	Phytochemical name	Pharmacological activity of plant	References
1	*Curcuma longa*	Haldi	Flavonoid	Anti-inflammatory, anticancer, hepato-protective	Sharma *et.al* 2013
2	*Withania somnifera*	Ashwagandha	Withanolides, steroidal lactones	Helps to treat Alzheimer's and Parkinson's disorders, helps to enhance memory and immunomodulatory, anti-cancerous and chemo preventive	Rathinamoorthy *et.al* 2014
3	*Catharanthus roseus*	Sadabahar	Alkaloids	Anticancer	Priyadarshini *et.al* 2012
4	*Azadirachta Indica*	Neem	Di and Tri terpenoids, limonoids	Blood purifier that prevents skin disease, anti-diabetic, inhibit colon cancer, anti-allergic	Gupta *et.al* 2014
5	*Piper nigrum*	Kali mirch	Dehydro-pipernonaline, piperidine	Helps to remove cough, purify lungs, used in weight loss with turmeric, epilepsy, anti-carcinogenic, anti-hyperlipidaemic	Kaushik *et.al* 2002
6	*Tinospora cordifolia*	Geloy	Tinosporin, isoquinoline alkaloids	Cardioprotective, anti-diabetic, immunomodulator, chemo preventive	Nisar *et.al* 2012
7	*Aloe vera*	Ghrit Kumari	ß-sitosterol, compesterol, emodin and aloin	Helps to nourish skin and hairs, anti-diabetic, has healing properties, shows antiseptic effects, anti-viral and antitumor	Mittal *et.al* 2014
8	*Phyllanthus emblica*	Amla	Emblicanin B, punigluconin and pedunculagin	Good for skin, eyes and hairs, antiviral, anticancer, antidiabetic, anticancer and hepatoprotective	Paarakh *et.al 2010*
9	*Cinchona robusta*	Quina	Quinine	Antiparasitic and helps to treat malaria	Paarakh *et.al* 2010
10	*Swertia chirata*	Chirayita	Amarogenitine, ophellic acid, sawertiamarine and mangeferin	Antiviral, hepato-renal protective and shows anti-diabetic effect	Krishnaa *et.al* 2004
11	*Allium sativum*	Lahsun	Allicin	Anti-inflammatory, cardioprotective (helps to maintain hypertension)	Joshi *et.al* 2005
12	*Bergenia ciliate*	Pakhenbhed	IS-01246	Anti-arthritis (helps to treat Rheumatoid)	Seyyed *et.al* 2012

Table 8. Commercially available plant derived medicines

Plant Name	Name of the drug
Colchicum autumnale L.	Colchicine
Filipendula ulmaria (L.) Maxim	Aspirin
Artemisia annua L.	Artemisinin
Camptotheca acuminate Decne	Camptothecin
Taxus brevifolia Nutt.	Paclitaxel
Artemisia annua L.	Artemisinin
Catharanthus roseus (L.) G. Don	Vinblastine and vincristine
Papaver somniferum L.	Codeine
Papaver somniferum L.	Papaverine
Cannabis sativa L.	Cannabidiol

used to cure anxiety, depression, cytotoxicity, and mutagenic disorders. However the use of this plant has been controversial as apart from its beneficial effects, it has potential side effects that are revealed by many studies, such as abdominal pain, nausea, angioedema, rash, and pruritus were reported in many patients after treatment (Manayi *et.al* 2015). Ziziphora species comprises a large number of flowering plants that belong to Lamiaceae family and further have been classified into 236 genera and 6900-7200 species. These plants are rich in essential oils or many secondary metabolites used in the field of pharmaceutical, medicinal, traditional, and folk medicines. This species is used to treat cold, fever, inflammation, intestinal disorders, insomnia, and cardiovascular malfunction for centuries (Mohammadhosseini *et.al* 2017). Secondary metabolites investigation on *Thymus alternates* showed that this species contains terpenoids, pentacyclic, and betulinic acid. The phytochemicals of this plant have been used as flavoring agents while for medicinal purpose it has been found effective against cancer cell lines (Acqua *et.al* 2017). *Phyllanthus Urinarica L.* genus belonging to Phyllantaceae family has been investigated as a rich source of lignans, tannins, flavonoids, phenolics, terpenoids, and other secondary metabolites. These secondary metabolites cure jaundice, diabetes, malaria, and liver disease. This plant also shows activity against cancer, microbial infections, and cardiovascular effects (Geethangili *et.al* 2018).

Some more investigations are there that represent the pharmacological activity of medicinal plants. *Ipomoea batata L.,* commonly known as sweet potato, is widely consumed all over the world. It has many beneficial effects on human health as it contains many vitamins and phytochemicals. These phytochemicals also reveal activity against cancer, diabetes, inflammation, and antioxidants. Sweet potato also contains beta-carotene and a precursor of vitamin A that helps to cure night blindness and overcome the deficiency of vitamin A (Ghasemzadeh *et.al* 2016). South Indian grass that belongs to *Cyperaceae* species possesses large number of secondary metabolites that belong to classes alkaloids, flavonoids, steroids, phenols, and quinones. Out of all the phytochemicals, this grass contains alkaloids in a large amount and also shows many pharmaceutical activities that cure microbial infections and inflammation (Babu *et.al* 2014). *Capparis spinosa* has lots of secondary metabolites that help to improve biomarkers of cardiovascular diseases and diabetes (Zhang *et.al* 2018). *Glycyrrhiza glabra* root revealed the presence of many phytochemicals. These phytochemicals are very beneficial for human health in the enhancement of memory, cures depression, helps to maintain the glucose level in the body, and shows many other pharmacological effects (Ali Esmail AL-Snafi 2018). *Ocimum sanctum L.* commonly known as Holy basil or Tulsi, is used in India as medicine since ancient times as it helps to improve stress, inflammation, and cancer (Sing *et.al* 2018, Siva *et.al* 2016).

Genus Macaranga Thou. Belongs to Euphorbiaceae that comprises 300 species of plants. These species are mainly found in the tropics of Africa, Australia, Pacific regions, and Asia. This genus is traditionally used to treat cuts,

sore, bruises, boils, and swelling (Magadula *et.al* 2014). *Pleurotus sajor caju* is commonly known as mushrooms, are great source of primary and secondary metabolites and contain about 40-49% of protein. Apart from this mushrooms have anticancer, antidiabetic, antibacterial, and anti-inflammation activities. Mushrooms also play an important role in healing (Devi *et.al* 2015). *Cymbopogan citratus stapf*, *Eugenia uniflora* leaves and *Citrullus vulgaris schard* also contain many primary and secondary metabolites that are reported by Geetha *et.al* 2014, Daniel *et.al* 2014 and Hannah *et.al* 2015. *Calophyllum Inophyllum* belongs to clusiaceae family and it occurs above the high tide mark along the sea coast of Northern Australia and expanding throughout South India and Ssouth-East Asia. This plant species contains lots of secondary metabolites in their root, stem, and leaves that help to fight against microbial infections, inflammation, and used in cosmetics (Sundur *et.al* 2014). *Morus alba* belongs to Moraceae family and contains many medicinal plants, and has numerous applications in various fields such as agriculture, food, cosmetic and pharmaceutical industries. Pharmacological activities of these plants help in the treatment of an inflammatory condition, gastrointestinal disorder, cancer, and microbial infections with the help of many secondary metabolites (Hussain *et.al* 2017). Another study was performed by B. J. Divya and other scientists in 2017 that worked on *Allium sativum*. *Allium sativum* belongs to the family Amaryllidaceae and commonly known as garlic. In this study, to extract secondary metabolites from garlic cloves different chemicals and techniques were used. Hexane, ethyl acetate, methanol and water revealed steroids, alkaloids, flavonoids and other bioactive compounds. These phytochemicals of garlic cloves have been used to treat several infections from ancient period.

Momordica diocca commonly known as Kakrol or spiny gourd is mainly found in India and Bangladesh, and is not only used as medicinal plant but also consumed as vegetable on a large scale. This plant consist of many minerals compositions, preventive, protective and curative agents in their root, stem and fruit. This plant includes many pharmacological activities such as anti-oxidant, analgesic, nephron protective, neuro protective, antiallergic, antimalarial, hepatoprotective and antihepatotoxic activity (Talukdar and Hossain 2014). *Genitina* is an important genus of Gentianaceae family that comprises 400 species and distributed all over the world. Based on investigation, this plant is used traditionally in Iran. This plant species consist lots of phytochemicals such as gentipicroside, xanthones, monoterpenes, alkaloids and flavonoids. This plant species has lots of promising bioactive agents are present that cure menstrual over bleeding, animal venom poisoning, infected wounds, injuries, vitiligo and swelling of liver, spleen, stomach and sprain of muscles (Mirzaee *et.al* 2017). Some more medicinal plants with their pharmacological activities are summarized in Table 7 given below.

By using advance research technologies, scientists are working hard to produce rich variety of phytochemicals under laboratory conditions using plant cell cultures (Yue *et.al* 2014). Guerriero *et.al* 2018, cultured *Artemisia*, *Coffea arabica L.* and *Urtica dioica L.* to produce large amount of secondary metabolites terpenoids, alkaloids and phenolic compounds respectively. Many trans genes such as *rol ABC* genes are also used by Kiani *et. al.* 2015, to increase the production of phytochemicals. Secondary metabolites are extracted from many plant species and used to make many drugs that cures different disorders. There are number of drugs that are composed of heterogenous phytochemicals and are available in market. Some of the drugs are enlisted in Table 8 (Garnatje *e.al* 2017). These drugs not only cure the diseases but also solve the problem of drug resistance and provide a new path for scientist to discover more drugs to fight against dreadful diseases (Anand *et.al* 2019).

CONCLUSION

Plants are a valuable resource that yields numerous phytochemicals which can be used as potential drugs to treat and prevent many human ailments and diseases. These drugs also provide a safer alternative to allopathic medicines overcoming the problems of drug resistance, toxicity and side effects. The bioactivity of plant extracts and their component phytochemicals have been studied extensively and put to use since ancient times. Novel approaches are now being explored for enhanced production and efficient

yielding of secondary metabolites through cell and tissue cultures. Advances in cell line culture allowing in-vitro bioactivity testing also opens avenues for faster drug development.

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Conflicts of Interest

The authors declare that there are no conflicts of interest.

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