An Overview of Various Piper Species for Their Biological Activities
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ABSTRACT
The genus Piper belongs to the family Piperaceae and has more than 2000 species. These plants are found almost all over the world. Some of these species are also found in India. In India these plants are mostly available in Northern part & North-Eastern part such as Himachal Pradesh, Arunachal Pradesh, Khasi and Jayantia hills of Meghalaya, Assam, Manipur. Piper is mostly known for its commercial, economical and medicinal importance. These plants contain many chemical constituents such as piperidine, chavincin, starch, protein, cineole, p-cymene, lignin, sesquiterpenes, piperolite, benzoic acid derivatives, schimidtin and carvone; even volatile oils such as terpenes, phellandrene, caryophyllene, piperonal-dihydrocarbeol and caryophyllene oxide are found to be very rich in these plants. Various activities such as antifeeding, antibacterial, antifungal, antiinflammatory, antiamaeobic, antiplatelets, insecticidal, antioxidant, cytotoxic, antiplasmodial, DNA damaging activities etc. are manifested by these plants. These plants are being utilized by many traditional medicinal system like Traditional Chinese Medicine, Indian Ayurvedic system and folklore medicine of Latin America. Some of these species are very much useful in preparation of spices like Piper nigrum which is known as the King of Spices and also enhance the bioavailability of food and drugs as a carminative. The fruits of Piper are used for the treatment of various diseases of respiratory tract viz. cough, bronchitis, asthma.

Keywords: Antimicrobial activity, ant-repellent activity, cytotoxic activity, insecticidal activity, piper, piperine

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INTRODUCTION
A large number of natural products are being used as traditional medicine in several countries for the treatment of various diseases [1]. The genus Piper belongs to the family Piperaceae and has over 2000 species [2]. The plant is indigenous to India. It grows wild mostly in Himachal Pradesh, Arunachal Pradesh, Khasi and Jayantia hills of Meghalaya, Assam and Manipur [3]. These plants grow in the form of erect or scadent (climbing) herbs, shrubs, or less frequently trees [1]. Piper species have been used in variety of traditional medicinal systems such as Traditional Chinese Medicine, the Indian Ayurvedic system and folklore medicine of Latin America and West Indies [4]. The plants of genus Piper are also used for many other purposes such as foods and spices, fish bait, fish poison, hallucinogens, insecticides, oils, ornaments, perfumes etc [1]. Piper species are of high commercial and economical importance such as Piper nigrum, it has world-wide spice market [5]. The phytoconstituents obtained from Piper species are characterized by the production of typical classes of compounds such as amides, benzoic acids, chromenes, terpenes, phenylpropanoids, lignans, other phenolics and a series of alkaloids [1]. They have shown antifeeding [3], antibacterial [6,7], antifungal [8,9], antiplatelet [10,11], antioxidant [11], anti-inflammatory [12], antiamoebic [13], insecticidal [14-16], cytotoxic [17-20], antiplasmodial [21] and DNA damaging activities [4].

Description
The different species of Piper are largely distributed in tropical and subtropical region of the world [22]. The plant is a
woody vine in nature and may ascend up to 20 feet. The plant is cultivated in India and other countries like Nepal, Indonesia, Sri Lanka, Brazil, Malaysia, Sumatra, China etc. The stems of the plant are mostly prostrate and thickened at nodes. The plant can be propagated either by cuttings or by seeds during rainy season. It starts bearing fruits after 7 to 8 years which can also survive up to 100 years [2].

Black pepper is initially green which become yellowish orange and finally turn to red when ripped. They are round-shaped with scar of stigmas at apex of each fruit. The surface of dried Piper fruit is uneven and wrinkled. It has an aromatic odour and pungent taste. The seeds have few testa floury albumen and hardened periphery [2].

**Fig. 1: Piper caninum**

**Fig. 2: Piper nigrum**

**Fig. 3: Piper lolot**

**Fig.4: Piper mullesua**

**Phytochemistry**

The literature survey had shown various phytoconstituents of different species of Piper where it was reported that black pepper contains piperine, pipereidine, chavicol, starch, protein, phellandrene, caryophyllene, cineole, p-cymene and carvone. Piperine was isolated as the main alkaloid from pepper. The presence of volatile oil consisting of terpenes, phellandrene, caryophyllene, piperonal-dihydrocarbeol and caryophyllene oxidesabene, myrecene, limonene, α & β pinenes, α-bengenotene, humulene, p-cymene and α-selinene in *Piper nigrum* was also reported. Lignans, cubebin was found only in *Piper cubeba*. Vitexin and marginatoside were found in the leaves of
Piper marginatum [2]. Myristicin, asarinin, sesamin and fargesin were found in Piper mullesua [3]. The presence of hydroxychavicol acetate, allylproocatehol-piperbetol, eugenol, isoeugenol, safrol, anethole, stearic acid, methyl eugenol, carvacrol, polyphenol, alkaloids, saponin, tannin, steroids and other compounds like chavicol, chavibetol, allylpyrocatechol, chavibetol acetate in Piper betle were mentioned [22]. The compound such as piperlotine A, piperlotine C, cinnamoylpyrrolidine, sermente, pellitorine were found in Piper lolot [10, 11]. The presence of new benzoic acid derivatives crassinervic acid, aduncumene, hostmaniane and gaudichaudianic acid in P. crassinervium, P. aduncum, P. hostmania-num and P. gaudichaudianum were reported [23]. The presence of tembamide acetate and alatamide into aerial parts of Piper guayranum were well documented [24]. The compounds such as pyridine alkaloid, piplartine and piplartine dimer were found in Piper aborescens [17].

![Phytoconstituents](image)

**Fig. 5: Structure of Phytoconstituents**

The presence of volatile oil, resin, alkaloids, calcium, phosphorous and iron into fruits of Piper were reported [2]. The components such as taboganic acid, pinocembrin, pinocembrinchalcone, lanceaefolic acid methyl ester in Piper lanceafolium were mentioned [9]. The presence of sakuranetin, anodendroic acid methyl ester and carotenoid lutein in Piper aduncum were reported [7].

**Extraction**

The solvents such as ethanol, methanol, chloroform, n-hexane, ethyl acetate, dichloromethane, acetone, petroleum ether, benzene and water were used for the extraction of various plant parts of Piper. Here the extraction scheme of different plant parts of Piper obtained from literature survey was shown below:
I. EXTRACTION OF LEAVES [9]

Air dried leaves of *Piper lanceafolium*

- Extracted with Acetone
- Concentrated to dryness
- Extracted with Methanol and water (3:1)

Fractionated by

- Hexane
- Butanol
- Chloroform
- Water
- Ethylacetate
- Ethanol

II. EXTRACTION OF ROOTS [25]

- Dried powder of *Piper nigrum* roots

- Extraction with methanol : water (7:3)
- Evaporation under vacuum

Extracted with

- Chloroform
- Ethyl acetate
- Butanol

III. EXTRACTION OF STEM [4]

- Dried stem of twigs of *Piper caninum*

- Extracted with dichloromethane : methanol (1:1)

IV. EXTRACTION OF FRUIT [26]

- Dried fruit of *Piper cubeba*

- Crushed into powder

- Extracted with water (Refluxed for 6 hours)

- Filtration

- Filtrate concentrated under pressure
The purification of fractions was done by silica gel column chromatography method with hexane-ethyl acetate and methanol.

**Biological Activities**

**Antifeeding activity:** Srivastav S et al. reported the ethanolic extract of *Piper mullesua* showed antifeeding activity against *Spilarctia obliqua* [3].

**Clastogenicity:** Junqueira APF et al. conducted an experiment to investigate the mutagenic potential of the crude extract of *Piper cubeba* seeds where peripheral blood and hepatic cells were collected for the comet assay and the bone marrow cells were collected for the micronucleus test [1].

**Antimicrobial activity:** Lugar P et al. investigated antimicrobial activity of the extract of the *Piper lolot* using n-hexane as a solvent. It was found that compound 3-(4’-Methoxyphenyl) propanoyl pyrrol of *Piper lolot* had shown antibacterial activity [6].

Orjala J et al. reported the petroleum ether extract of leaves of *Piper gibilimbum* had antibacterial activity against *Staphylococcus epidermidis* and *Bacillus cereus* [20]. The crude dichloromethane extract of the leaves of *Piper aduncum* was screened for its antibacterial activity against *Bacillus subtilis*, *Micrococcus luteus* and *Escherichia coli* [7]. Liu HX et al. reported antimicrobial activity against *Escherichia coli*, *Staphylococcus aureus* and *Candida albicans* of methanolic extract of *Piper nudibaccatum* [27]. Evans PH et al. reported antifungal activity of chloroform extract of *Piper betle* leaves against *Phytophthora ultimum* [8]. Alecio AC et al. mentioned the antifungal activity against *C. sphaerospermum* of dichloromethane extract of *Piper hispidum* leaves [9]. Lago JHG et al. reported antifungal activity of methanolic extract of *Piper crassinnervium* leaves against *C. cladosporioides* and *Cladosporium sphaerospermum* [23].

**Antiplatelet activity:** Lei D et al. reported antiplatelet activity of aqueous extract of inflorescence *Piper betle*, where inflorescence *Piper betle* inhibited the arachidonic acid induced and collagen-induced platelet aggregation [11]. Li CY et al. also mentioned that the methanolic extract of *Piper lolot* showed potent inhibitory activity on platelet aggregation [10].

**CYP3A4 inhibitory effect:** Usia T et al. mentioned the potent inhibitory activity of aqueous extract of *Piper cubeba* on the metabolism mediated by CYP3A4 enzyme. Human liver microsome was used for CYP inhibitory assay. The inhibitory activity on the metabolism mediated by CYP3A4 in vitro was determined using a radiometric measurement [26].

**Insecticidal activity:** Jensen HR et al. mentioned insecticidal activity of ethyl acetate extract of *Piper nigrum* seeds [14]. Chauvet DC et al. reported insecticidal activity of ethanolic extract of *Piper decurrens* leaves [15]. Miranda RP et al. conducted a study of chloroform extract of *Piper gunicastensis* leaves for its insecticidal activity [16].

**Antiamoebic activity:** Joshi Net al. reported antiamoebic activity of hexane fraction of ethanolic extract of *Piper schimidtii* [13].

**Antioxidant activity:** Lei D et al. mentioned antioxidant activity of aqueous extract of *Piper betle* inflorescence [11].

**DNA damaging activity:** Ma J et al. reported DNA damaging activity of dichloromethane–methanol (1:1) extract of *Piper canum* [4].

**Cytotoxic activity:** Duh CY et al. reported cytotoxic activity of chloroform extracts of *Piper aborescens* leaves [17]. Tang GH et al. mentioned cytotoxic activity of amide alkaloid obtained from methanolic extract of *Piper boehmeriaeifolium* [18]. Pan L et al. reported cytotoxic activity of chloroform extract of *Piper sermentosum* [19]. Mata R et al. reported cytotoxic activity of dichloromethane–methanol (1:1) extract of *Piper sancatum* leaves [28].

**Anti-inflammatory activity:** Lin LC et al. mentioned anti-inflammatory activity of methanolic extract of *Piper kadsura* stem [12].

**Antiplasmodial activity:** Flores N et al. reported antiplasmodial activity against *Plasmodium falciparum* of ethanolic extract of *Piper glabratum* leaves [20].

**Ant repellent activity:** Capron MA et al. reported ant repellent activity of chloroform fraction of hexane extract of *Piper tuberculatum* leaves [29]. Green TP et al. also reported ant repellent activity of
chloroform extract of *Piper arieanum* leaves [30].

**Table 1: Biological Activities of Various Piper Species**

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Species</th>
<th>Solvents used</th>
<th>Plant part</th>
<th>Biological Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td><em>Piper aborescens</em> [17]</td>
<td>Methanol, Chloroform, Water</td>
<td>Leaves</td>
<td>Cytotoxicity against the KB nasopharyngeal carcinoma and p388 lymphocytic leukaemia system.</td>
</tr>
<tr>
<td>03</td>
<td><em>Piper arieianum</em> [30]</td>
<td>Methanol, Chloroform, Water</td>
<td>Leaves</td>
<td>Ant repellent</td>
</tr>
<tr>
<td>04</td>
<td><em>Piper betle</em> [8,11]</td>
<td>Chloroform, Water</td>
<td>Leaves, Inflorescence</td>
<td>Fungicidal and Nematocidal, Antioxidative and Antiplatelet</td>
</tr>
<tr>
<td>05</td>
<td><em>Piper boehmeriaefolium</em> [18]</td>
<td>Methanol, Petroleum ether, Chloroform</td>
<td>Whole Plant</td>
<td>Cytotoxic activity</td>
</tr>
<tr>
<td>06</td>
<td><em>Piper caninum</em> [4]</td>
<td>Dichloromethane-Methanol (1:1)</td>
<td>Stem of twigs</td>
<td>DNA damaging activity</td>
</tr>
<tr>
<td>07</td>
<td><em>Piper crassinervium</em> [23]</td>
<td>Methanol</td>
<td>Leaves</td>
<td>Fungitoxic activity against <em>C. cladosporioides</em> and <em>C. sphaerospermum</em>.</td>
</tr>
<tr>
<td>08</td>
<td><em>Piper cubeba</em> [1,26]</td>
<td>Ethanol, Water, Ethyl acetate, Methanol</td>
<td>Seed, Dried fruit</td>
<td>CYP3A4 inhibitory effect</td>
</tr>
<tr>
<td>09</td>
<td><em>Piper decurrens</em> [15]</td>
<td>Ethanol</td>
<td>Leaves</td>
<td>Larvicidal activity against <em>O. nubilalis</em> and <em>A. atropalpus</em>.</td>
</tr>
<tr>
<td>12</td>
<td><em>Piper guanacastensis</em> [16]</td>
<td>Ethanol, Hexane, Chloroform, Butanol</td>
<td>Leaves</td>
<td>Insecticidal activity against <em>Aedes atropalpus</em> mosquito larvae</td>
</tr>
<tr>
<td>14</td>
<td><em>Piper kadsura</em> [12]</td>
<td>Methanol, Stems</td>
<td></td>
<td>Antinflammatory &amp;</td>
</tr>
</tbody>
</table>
CONCLUSION
From the present study it has been observed that many medicinally active species of Piper are available all over the world. These can be beneficially used for the treatment of different types of ailments. These plants are mainly used as antibacterial, antifungal, antiplatelets, insecticidal, antioxidants, ant-repellent, antiamoebic, antifeeding, anti-inflammatory, antiplasmodial etc. This paper can be a guideline for those researchers who are involved in the research of different Piper species. The further study can be conducted to formulate new different forms of medicine of various Piper species. There is a great scope in studying all these natural herbs for the

<table>
<thead>
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<th>No.</th>
<th>Species</th>
<th>Extracts</th>
<th>Parts</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td><em>Piper lanceafolium</em> [31]</td>
<td>Chloroform, n-Butanol, Water, Acetone, Hexane, Chloroform, Ethyl ether</td>
<td>Leaves</td>
<td>Immuno-modulatory activity</td>
</tr>
<tr>
<td>16</td>
<td><em>Piper lolot</em> [6,10]</td>
<td>Chloroform, n-hexane</td>
<td>Rhizomes</td>
<td>Antifungal activity</td>
</tr>
<tr>
<td>18</td>
<td><em>Piper nigrum</em> [14]</td>
<td>Ethyl acetate</td>
<td>Seeds</td>
<td>Insecticidal</td>
</tr>
<tr>
<td>19</td>
<td><em>Piper nudibaccatum</em> [27]</td>
<td>Methanol, Petroleum ether, Chloroform, Water</td>
<td>Aerial parts</td>
<td>Antimicrobial activity against <em>E. coli and S. aureus.</em></td>
</tr>
<tr>
<td>21</td>
<td><em>Piper sanctum</em> [28]</td>
<td>Dichloromethane, Methanol, Petroleum ether, Water</td>
<td>Leaves</td>
<td>Antimicrobial activity against <em>M. tuberculosis,</em> Cytotoxicity assay against vero cells.</td>
</tr>
<tr>
<td>24</td>
<td><em>Piper tuberculatum</em> [29]</td>
<td>Chloroform, Hexane</td>
<td>Leaves</td>
<td>Ant repellent.</td>
</tr>
</tbody>
</table>
development of potent pharmaceuticals in the future.

REFERENCES


23. Lago JHG, Ramos CS, Casanova DC, Morandim AA, Bergame DC, Cavalheiro Al et al. Benzoic Acid Derivatives from Piper Species and Their Fungitoxic Activity against Cladosporium cladosporioides and C.


