CHAPTER - I

INTRODUCTION
Since, the time of creation of the planet "earth", plant kingdom has fed the entire world and cured several ills and is still doing so. A vast knowledge of medicinal plants must therefore have been accumulated, especially in India, where various plants of medicinal importance are found.

From ancient times, up to date, people healed themselves with traditional herbal medicines which in several cases, by trial and error, proved efficaceous. In the recent past one could notice a global trend for the revival of interest in the traditional system of medicines. In the mean time W.H.O. has impressed upon the support and encouragement on a global basis, to the traditional system of medicine and urged upon the Governments of S.E. Asian region to pay importance to the development of this system as a close adjunct, to the modern medicine so as to achieve the proclaimed goal of health for all people.

Screening of medicinal herbs has become a potential source of bio-dynamic compounds of therapeutic values in phytochemical researches. Ethnobotanists bring out suggestions as to which plant material may be tapped and for which they get
clues from rural or tribal men. This field has received considerable attention in India as well as abroad\textsuperscript{1-10}.

The purpose of the study is to point out the potentials of medicinal plants and to explore the possibility of finding and improving new uses of plants of the area. It is worthwhile to tap traditional knowledge while the elderly medicinal men, who are familiar with curative values of plants, are still alive.

Chemical investigations in the field of natural products aims at exploring the bio-chemical potential of the flora of Indian subcontinent for their bioactive constituents.

Discoveries in this field is complemented by the investigations on bio-synthesis and biotransformation. A systematic screening of plant extracts for their bio-active constituents has resulted in the isolation of various plant metabolites, e.g., steroids, flavonoids, xanthons, coumarins, alkaloids, terpenes and glycosides etc.

The Indian subcontinent is a vast source of plants; which attracts the scientists across
the world, dedicated to the task of ameliorating human sufferings. As such, it was realised that in the field of medical science it will be appropriate to develop our own indigenous expertise and technology for the manufacture of cheaper drugs of greater potential therapeutic importance for which may be necessarily be affordable by common men of rural segment of the nation.

The excessive development in the field of flavonoids and isoflavonoids has been mainly due to several advances in the chromatographic techniques and spectroscopic analysis.

Still, chromatographic techniques like TLC\textsuperscript{11,12}, paper\textsuperscript{13,14} and column chromatography\textsuperscript{15,16} are in frequent use. A number of new chromatographic techniques have been developed for the identification of flavonoids. Some of them are of greater importance for resolving glycosidic mixture e.g. Droplet-counter current-chromatographic technique developed by Tarimura\textsuperscript{17}. The other most important technique is HPLC being used in separation of complex mixtures. Several workers have reported the importance of HPLC for the separation of phenolics\textsuperscript{18,19} of plants including flavonoids.
UV spectroscopy has become a major technique for the structural analysis of flavonoids. The position of OH/OMe/sugars are fixed by the use of various shift reagents\(^\text{20}\).

The Infra-red spectrum provides a valuable information about the functional group in a given environment.

Proton magnetic resonance is very useful for the determination of structural environment of proton conformations, chemical shift & population trends. In NMR, various paramagnetic shifts are of immense help in the study of sugar position, prenylation and hydroxylation\(^\text{21-24}\).

\(^{13}\text{C}-\text{NMR}\) provides information relating to the carbon backbone of the molecule. The different types of aglycones are distinguishable on the basis of aromatic carbon resonance but chemical shift for central three carbon units are often quite distinctive. Acetylation of free phenolic hydroxy group produces marked changes in \(^{13}\text{C}\) NMR of flavonoids and used to detect the location of \(-\text{OH}\) groups\(^\text{25}\).

Mass spectroscopy\(^\text{26-29}\) has been used for determination of molecular weight and also provides fragmentation pattern. Flavonoidal glycosides
possess characteristic fragmentation pattern\textsuperscript{30}. Many workers have discussed fragmentation pattern of the methoxy and hydroxy flavonoids\textsuperscript{31-38}.

Bio-active constituents obtained as plant isolates may be useful directly or may serve as starting materials for the synthesis of active agents\textsuperscript{39-42}.

Numerous physiological activities have been attributed to flavonoids\textsuperscript{43}, including frequently reported mutagenic and less frequently reported antimutagenic activities\textsuperscript{45,46}. Flavonoids are consumed in measurable amount by humans. Estimated daily dietary intake is 1 gm/day in the United States\textsuperscript{47}.

Previously, many flavonoids have been showed anticarcinogenic activity\textsuperscript{48}. Van Durran and co-workers\textsuperscript{49,50} showed that the flavonoids rutin, morin and quercetin inhibited tumorigenesis by benzo (a) pyrene in mouse skin\textsuperscript{51}.

Few flavonoids have been demonstrated to inhibit tumour promotion. Quercetin inhibited tumour promotion by 12-O-tetradecanoyl, phorobol-13-acetate in a mouse skin promotion assay\textsuperscript{52}. Eupatin and Eupatoretin\textsuperscript{53} are moderately effective against carcinoma of nasopharynx.
Most of the flavonoids show a marked degree of toxicity against both the bacteria and fungi. The antifugal activity\textsuperscript{54} may primarily be due to the presence of $\gamma$-pyrone ring.

Yoshinori Tsuchiya et al.\textsuperscript{55} have isolated chrysosplenol B and chrysosplenol C, which showed antiviral activity especially against rhinovirus.

Flavonoids are known to inhibit many enzymes such as phosphodiesterase\textsuperscript{56-58}, Ca\textsuperscript{2+} AT pace\textsuperscript{59}, aldose, reductase\textsuperscript{60-62}, lipoxygenase\textsuperscript{63,64} and cyclooxygenase\textsuperscript{65}.

The isoflavonoids are biogenetically relative to flavonoid. They are isomeric with flavone and differ only in attachment of aryl (B) ring to central pyran nucleus. Common isoflavone has usual 5,7,4' or 3'4' hydroxylation pattern but there are also several rarer isoflavones.

It is therefore felt necessary to carry out a systematic phytochemical investigations of the unexplored national flora having reputed therapeutic importance in order to reveal the secret of their physiological importance.

An attempt has therefore been made to carry out phytochemical studies of some Cucurbitaceae
plants. Cucurbitaceae family comprises of 34 genera and 108 species in India. 

Cucumis momordica \(^{67-69}\) worked up in 1976 by Tondon et al. \(^{70}\), who isolated the oil from its seeds kernels and found it to consist of fatty acids. They also characterised the seed oil of cucumis utilissimus in 1977 \(^{71}\) and noticed that high percentage of unsaturated fatty acids might possibly be responsible for its cooling effect which is characteristic of Cucurbitaceae family.

\(^{72,73}\) C. Rimington et al. have isolated many compounds from different species of cucumis e.g. C.africanus, C.myriocarpus, C.leptodermin, which were found to be fish poisons.

A thorough survey of literature has revealed that significantly inadequate phytochemical work has been reported on the cucurbitaceae plants and their still remains enough scope for further systematic phytochemical investigations.

The following two plants: (1) Trichosanthes anguina Linn. and (2) Coccinia indica W&A were taken for phytochemically investigations because of their therapeutic values against dreadful diseases in order to isolate their bio-active constituents, which
could possibly be utilised as potential drugs and as intermediates for the production of important therapeutic agents.

1. **Trichosanthes anguina** Linn : Trichosanthes anguina Linn.\(^7^4\) (N.O. Cucurbitaceae) is commonly known as "chachinda" in Hindi which is found in the hotter parts of India and China. The Ayurvedic system of medicine describes, the plant is useful in the treatment of cough, biliousness and used as purgative and anthelmintic. It's seeds are used as antidiarrhoeal and also used in the treatment of syphilis\(^7^5\).

2. **Coccinia indica** W&A : Coccinia indica W&A\(^7^6\) (N.O. Cucurbitaceae) is commonly known as "Kundru" in Hindi. It is found throughout in India.

   It's roots is cooling\(^7^7,7^8\) and useful to stops vomiting, urinary losses. The leaves of this plant cures 'Kapha' and 'Pitta'. The flowers are used in the treatment of itching, biliousness and jaundice. The fruits are used as antipyretic and cures, leprosy, bronchitis and asthma.

   The plant C.indica contains an enzyme with amylolytic properties, a harmone and traces of an alkaloid. Fresh juice extracted from the leaves, stem and root of the plant produces no reduction
of sugar in blood or urine of patients suffering from glycosuria.

The details of various investigations on the bio-active constituents of some Cucurbitaceae species by earlier workers, are summarised in the Table-I.

Some of the recently investigated biologically active flavonoids and isoflavonoids from other families are listed below:

I. New flavonol glycoside from Epimedium acuminatum.\(^9^9\).

II. Flavonoids of Asteriscus gravoelens.\(^9^0\).

III. Plant anticancer agent, new cytotoxic flavonoids from muntingia calabura roots.\(^9^1\).

IV. Antihyperlipidemic effect of flavonoids from prunus davidiana.\(^9^2\).

V. Isoflavone glycoside from Neorautanenia amboensis.\(^9^2\).

VI. Flavonoids with anticataract activity from Brickella arguta.\(^9^4\).

VII. Isolation and cytotoxicity of two new flavonoids from Chrysoplenium grayanum.\(^9^5\).

VIII. A new Quercetin-Acyl glucuronide from Scolymus hispanicus.\(^9^6\).
<table>
<thead>
<tr>
<th>S. No.</th>
<th>PLANT</th>
<th>PART</th>
<th>COMPOUND ISOLATED</th>
<th>REFERENCES</th>
<th>STRUCTURE</th>
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<tbody>
<tr>
<td>1.</td>
<td>Cucumis melo</td>
<td>-</td>
<td>Isovitexin 2&quot;-O-glucoside</td>
<td>79</td>
<td>I</td>
</tr>
<tr>
<td>2.</td>
<td>Cucumis melo</td>
<td>-</td>
<td>Isovitexin-X&quot;-O-trans-caffeoyl-2&quot;-O-glucoside</td>
<td>79</td>
<td>II</td>
</tr>
<tr>
<td>3.</td>
<td>Cucumis melo</td>
<td>-</td>
<td>Isoorientin-2&quot;-O-glucoside</td>
<td>79</td>
<td>III</td>
</tr>
<tr>
<td>4.</td>
<td>Cucumis melo</td>
<td>-</td>
<td>Isoorientin-2&quot;-O-trans-caffeoyl-glycoside</td>
<td>79</td>
<td>IV</td>
</tr>
<tr>
<td>5.</td>
<td>Mormordica charantia</td>
<td>Leaves</td>
<td>Cucurbitane Triterpenoids</td>
<td>80</td>
<td>V-a, V-b, V-c</td>
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<tr>
<td>6.</td>
<td>Fevillea trilobata</td>
<td>-</td>
<td>Norcucurbitacin and Heptanoxy cucurbitacin glucosides</td>
<td>81</td>
<td>VI</td>
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<td>7.</td>
<td>Cucurbita pepo.L.</td>
<td>Fruits</td>
<td>Cucurbitacins (Esterases)</td>
<td>82</td>
<td>VII-a, VII-b, VII-c</td>
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<td>8.</td>
<td>Trichosa-nthes japonica</td>
<td>Roots</td>
<td>C-24 Epimeric 24-Ethyl-D-sterols</td>
<td>83</td>
<td>VIII</td>
</tr>
<tr>
<td>9.</td>
<td>Lagenaria breviflora</td>
<td>Fruits</td>
<td>Triterpenoid saponins</td>
<td>84</td>
<td>IX</td>
</tr>
<tr>
<td>10.</td>
<td>Coccinia indica</td>
<td>Roots</td>
<td>β-amyrin β-sitosterol</td>
<td>85</td>
<td>X-a, X-b</td>
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<tr>
<td>11.</td>
<td>Trichosa-nthes anguina</td>
<td>Seeds</td>
<td>Folic acid</td>
<td>86</td>
<td></td>
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<tr>
<td>12.</td>
<td>Trichosa-nthes anguina</td>
<td>Fruits</td>
<td>Phenolic constituents, Quercetin</td>
<td>87</td>
<td>XI</td>
</tr>
<tr>
<td>13.</td>
<td>Trichosa-nthes anguina</td>
<td>Seeds</td>
<td>Lectin, glycoprotein</td>
<td>88</td>
<td>-</td>
</tr>
</tbody>
</table>
2'-O-Glucoside

(I)

X'-O-trans-caffeoyl-2'-O-glucoside

(II)
(III)

2'-O-Glucoside

(IV)

2'-O-trans-caffeylglucoside
(V-a)

R = H

(V-b)

$R^1, R^2, R^3 = H$
\[ R^1, R^2 = H, \quad R^3 = Me \]

(V-c)

(VI)
Cucurbitacin B : R=OAc
Cucurbitacin D : R=H

(VII-a)

Cucurbitacin E : R=OAc
Cucurbitacin I : R=H

(VII-b)
Cucurbitacin A : R=OAc
Cucurbitacin N : R=H

(VII-c)

(VIII)
(IX)

(X-a)
IX. 7,2',4'-trihydroxy-3'-methoxy isoflavone from Zollernia paraensis.97

X. Three new prenyl flavones from Actocarpus altilis.98

Thus, a deep sweep in the available literature on the Cucurbitaceae plants has revealed that there is still enough scope for further systematic phytochemical investigations on (1) Trichasanthes anguina Linn. and (2) Coccinia indica W&A (N.O. Cucurbitaceae).

Hence the authoress took up the challenging task of phytochemically investigating the bio-active constituents of these plants and her findings are summarised below:
PROBLEM TAKEN AND WORK DONE

Plants are very essential for maintenance of habitable environment for human life and for sustaining all animals life on the planet.

Therefore adequate knowledge of plants is essential in the country like India where the medicinal flora is rich in diversity and endemism.

At the present time a world wide research is on for the discovery of those drugs, which may potentially be utilised to conquer those diseases which have yet remained unconquered like carcinoma and leukemia etc.

Thus there is an imperative need to have expertise knowledge about medicinally important plants, by the scientists working on natural products.

The authouress therefore thought worthwhile to investigate the plants: (1) *Trichosanthes anguina* (N.O. Cucurbitaceae) and (2) *Coccinia indica* (N.O. Cucurbitaceae), phytochemically for their bio-active constituents (flavonoidal and isoflavonoidal) and her findings are summarised below:
I. ISOLATION AND CHARACTERISATION OF A NOVEL FLAVONE GLYCOSIDE: 5,6-DIHYDROXY-7,8,3'-TRIMETHOXY FLAVONE-4'-O-β-D-XYLOFURANOSYL (1→4)-O-β-D-GLUCOPYRANOSIDE FROM THE SEEDS OF TRICHOSEANTHES ANGUINA LINN.

The study of novel flavone glycoside (yield 0.065%), molecular formula: \( \text{C}_{29}\text{H}_{34}\text{O}_{17} \), m.p. 336°C, and \( M^+ 654 \) (EIMS), obtained from the EtOAc soluble fraction of the concentrated ethanolic extract of the seeds of *Trichosanthes anguina* Linn. has been described in this chapter.

It has been identified as; 5,6-dihydroxy-7,8,3'-trimethoxy flavone-4'-O-β-D-xylofuranosyl (1→4)-O-β-D-glucopyranoside (I), by various colour reactions, chemical degradations and spectral data.
II. ISOLATION AND CHARACTERISATION OF A NOVEL FLAVONE GLYCOSIDE; 7-HYDROXY, 6-METHOXY-5-O-α-L-RHAMNOPYRANO-SIDE FROM THE SEEDS OF TRICHOSANTHES ANGUINA LINN.

This chapter includes the study of a novel flavone glycoside (yield 0.068%) molecular formula \( \text{C}_{22}\text{H}_{22}\text{O}_{9} \); m.p. 327 °C, \([\text{M}]^+ 430\) (EIMS), obtained from the EtOAc soluble fraction of the concentrated ethanolic extract of the seeds of *Trichosanthes anguina* Linn. It has been identified as 7-hydroxy, 6-methoxy-5-O-α-L-rhamnopyranoside (II) on the basis of various colour reactions, chemical degradations and spectral analysis.
III. ISOLATION AND CHARACTERISATION OF A NOVEL ISOFLAVONE GLYCOSIDE; 5,6,6'-'TRIMETHOXY-3'4'-METHYLENEDIOXY ISOFLAVONE, 7-O-β-D-(2"-O-p-COUMAROYL) GLUCOPYRANO-SIDE, FROM THE SEEDS OF TRICHOSANTHES ANGUINA LINN.

The AcOH soluble fraction of the concentrated ethanolic extract of the seeds of Trichosanthes anguina Linn., yielded a isoflavone glycoside (yield 0.066%) molecular formula C_{34}H_{32}O_{15}; m.p. 165°C and M^+ 680 (EIMS). Its structure has been determined by the different colour reactions, chemical degradation and spectroscopic analysis as; 5,6,6'-trimethoxy-3'4'-methylenedioxy isoflavone 7-O-β-D-(2"-O-p-coumaroyl) glucopyranoside (III).
IV. ISOLATION AND CHARACTERISATION OF A NOVEL FLAVONE GLYCOSIDE: 6-METHYL, 7-METHOXY FLAVANONE, 5-O-\(\alpha\)-L-RHAMNOPYRANOSYL (1\(\rightarrow\)4)-O-\(\beta\)-D-GLUCOPYRANOSIDE FROM THE AERIAL PARTS OF COCCINIA INDICA W&A

The isolation and structural eludication of a novel flavanone glycoside (yield 0.056\%), molecular formula C\(_{29}\)H\(_{36}\)O\(_{13}\); m.p. 300\(^\circ\)C and [M]\(^+\) 592 (EIMS) obtained from the EtOAc soluble fraction of the concentrated methanolic extract of the aerial part of Coccinia indica W&A, has been dealt in this chapter. It has been identified as; 6-methyl-7-methoxy-flavanone-5-O-\(\alpha\)-L-rhamnopyanosyl (1\(\rightarrow\)4)-O-\(\beta\)-D-glucopyranoside (IV) on the basis of different colour reactions chemical degradations and spectral studies.
REFERENCES


74. Wealth of India, A Dictionary of Indian Raw Material and Industrial Products, CSIR Publ., New Delhi, 247 (1950).


76. Wealth of India, A Dictionary of Indian Raw Material and Industrial Products, CSIR Publ., New Delhi, 277 (1950).


