CHAPTER - I
INTRODUCTION
Despite the advent of enormous global development in medicinal education and modern medical facilities, the tribals' faith in the supernatural power of medicinal herbs persists up to date.

Though the belief that diseases were caused by hostile spirits due to violation of a taboo and lessened to some degree, the tribal system of medical treatment continuous to be a combination of "magic and medicine".

The changing pattern of life, living, food habits and the current trend of stress and strain on an individual has reached to such an optimum stage that the cardiac ailments have been growing at alarming rate and are claiming a major fragment of good talents untimely.

As such a stage has reached when the scientist should sit together to formulate a global strategy to rule out cardiac problem and discover suitable cardiac active substitutes.
The most common herbs used by the tribals were tulsi leaves for cure of epilepsy, mango for childrens diseases, mahua juice for malaria, Jack fruit (root) for gout and arthritis and tamarind seed for snake bite.

The Indian subcontinent due to its varied climatic condition is bestowed with unique medicinal flora with plants of economic value, yet to be "domesticated" and utilised for the benefit of human being.

According to the recent report of the Director General (ICMR), so far man has used about 3000 plant species for food and other purposes and only 150 have been commercially exploited all over the world. The tendency had been to concentrate on fewer species and today man depends only on 20-25 crop species. This was contrary to talk for diversification of crops.

Cardiac glycosides are a fascinating series of natural products that have been isolated from both plants and animals. Some members of this group of heart poisons are serving as important clinical agents. The cardiotonic property is associated with special structure of aglycone but is modified in regard to solubility and the nature of conjugated residue. Their administration in cases of impaired heart function leads to decreased rate and increased intensity of the heart beat, whilst their overdosage produces systolic stoppage of the heart. In
addition to use in cardiological some glycosides have been used as drugs in trials by ordeal and as an arrow poisons\textsuperscript{1}. Reviews on the chemistry, botanical distri-
bution and metabolism of the glycosides and aglycones are available\textsuperscript{2,3}.

Two groups of naturally occurring steroids are characterized by their ability to exert a specific and powerful action on the cardiac muscle of man. The number of one group are products of plant synthesis found in seed and bark while those of second group are elaborated in the organism of the toad and are found in skin secretions of the animal\textsuperscript{4}. The plant heart poisons are glycosides and on hydrolysis yield sugar free substances described as cardiac aglycone or genin. For example digitoxin is hydrolyzed to digitoxigenin and rare sugar digitoxose\textsuperscript{5}.

A very small amount of a cardiac principle can exert a beneficial action on the diseased heart while an excessive dose causes death. The active principles occur in various plants having a wide geographical distribution, particularly those of the order Apocynaceae, while others have been found in the Scrophulariaceae, Liliaceae and Ranunculaceae. Many species grow in tropical regions and have been used as arrow poisons\textsuperscript{6}. Digitalis plants such as the foxglove were used in the preparation of poisons for the medieval
ordeal and drugs made from the dried leaves of the plants have long been used as remedies. Digitalis was first employed for the treatment of dropsy\textsuperscript{7} and it later met with spectacular success in heart therapy. The pharmaceutical preparations of digitalis come from the seeds and leaves of Digitalis purpurea\textsuperscript{8}.

(A deep survey of available literature exhibits that search has been on for the discovery of cardiac active constituents of plant origin.)

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Plant</th>
<th>Cardenolides</th>
<th>Structure</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Strophanthus sarmentosus</td>
<td>Sarverogenin</td>
<td>I</td>
<td>9</td>
</tr>
<tr>
<td>2</td>
<td>Streblus asper</td>
<td>Asperoside</td>
<td>II</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kamaloside</td>
<td>III</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Strebloside</td>
<td>IV</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>Asclepias syrica</td>
<td>Syriobioside</td>
<td>V</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Syrioside</td>
<td>VI</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Uzarigenin</td>
<td>VII</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Desglucosyrioside</td>
<td>VIII</td>
<td>16</td>
</tr>
<tr>
<td>4</td>
<td>Calotropis procera</td>
<td>Calotropagenin</td>
<td>IX</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Uscharidin</td>
<td>X</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Voruscharin</td>
<td>XI</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Uscharin</td>
<td>XII</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Calactin</td>
<td>XIII</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gomphoside</td>
<td>XIV</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Calotoxin</td>
<td>XV</td>
<td>23</td>
</tr>
<tr>
<td>5</td>
<td>Gomphocarpus faruticosus</td>
<td>Gomphogenin</td>
<td>XVI</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Calotoxin</td>
<td>XV</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proceoside</td>
<td>XVII</td>
<td>26</td>
</tr>
<tr>
<td>6</td>
<td>Marsdenia erecta</td>
<td>Coroglaciaigenin</td>
<td>XVIII</td>
<td>27</td>
</tr>
</tbody>
</table>
Let us therefore exploit the resources of nature for the betterment of mankind which the creator has provided us and need to be used judiciously with discretion, in particularly in a country like India which is known all over the world for its abundance in natural wealth especially the cardiotonic drugs. A deep sweep in the available literature on some Liliaceae plants by the author revealed that still there was much scope of phytochemical investigations on the plants:

(1) Convallaria majalis : Linn.\textsuperscript{28} and
(2) Urginea indica : Roxb.\textsuperscript{29,30}

Convallaria majalis Linn. is a small glabrous herb abundantly found throughout the plains of India. It is cultivated in India as winter flowering herb. The rhizomes are pear shaped and about 5 cm. long. Convallaria majalis possesses cardiotonic, stimulant, expectorant, and diuretic properties\textsuperscript{31}.

T. Reichstein et al.\textsuperscript{32,33} have reported the presence of following cardiac glycosides from Convallaria majalis as described in Table-1.
<table>
<thead>
<tr>
<th>S. No.</th>
<th>Name of the glycoside</th>
<th>Name of the aglycone</th>
<th>Sugar</th>
<th>Source</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Convallatoxin (I)</td>
<td>Strophanthidin</td>
<td>L-Rhamnose</td>
<td>Convallaria majalis (Leaves)</td>
<td>34,35</td>
</tr>
<tr>
<td>2.</td>
<td>Convallloside (II)</td>
<td>--,--</td>
<td>L-Rhamnose + D-glucose</td>
<td>--,--</td>
<td>36,37</td>
</tr>
<tr>
<td>3.</td>
<td>Glucoconvallloside (III)</td>
<td>--,--</td>
<td>L-Rhamnose + 2D-glucose</td>
<td>--,--</td>
<td>38,39,40</td>
</tr>
<tr>
<td>4.</td>
<td>Convallatoxol (IV)</td>
<td>Strophanthidol</td>
<td>L-Rhamnose</td>
<td>--,--</td>
<td>41</td>
</tr>
<tr>
<td>5.</td>
<td>Convallatoxotoside (V)</td>
<td>--,--</td>
<td>L-Rhamnose + D-glucose</td>
<td>--,--</td>
<td>42</td>
</tr>
<tr>
<td>6.</td>
<td>Glucoperigulomethylloside (VI)</td>
<td>Periplogenin</td>
<td>Methyl - D-glucose + D-glucose</td>
<td>--,--</td>
<td>43</td>
</tr>
</tbody>
</table>
The another plant chosen by the author is *Urginea indica* Roxb. which is found in throughout the plains of India. Its bulbs are pear shaped and about 5 cm. long. It possesses cardiotonic, stimulant, expectorant and diuretic properties\(^{44}\).

Von Arthur Stoll et al.\(^{45}\) have reported the presence of following scilla glycosides from *Urginea indica* which are described in Table-2.
<table>
<thead>
<tr>
<th>S. No.</th>
<th>Name of the glycoside</th>
<th>Name of the aglycone</th>
<th>Sugar</th>
<th>Source</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Proscillaridin (I)</td>
<td>Scillarenin</td>
<td>L-Rhamnose</td>
<td>Urginea indica (Leaves)</td>
<td>46,47</td>
</tr>
<tr>
<td>2.</td>
<td>Scillaren A (II)</td>
<td>--,--</td>
<td>L-Rhamnose + D-glucose</td>
<td>--,--</td>
<td>48,49</td>
</tr>
<tr>
<td>3.</td>
<td>Glucoscillaren (III)</td>
<td>--,--</td>
<td>L-Rhamnose + 2D-glucose</td>
<td>--,--</td>
<td>50</td>
</tr>
<tr>
<td>4.</td>
<td>Scilliroside (IV)</td>
<td>Scillirosidin</td>
<td>D-glucose</td>
<td>--,--</td>
<td>51,52</td>
</tr>
</tbody>
</table>
The above discussion clearly transpired that the plant (i) *Convallaria majalis* Linn. and (ii) *Urginea indica* Roxb. have not yet been investigated systematically. Therefore the author took up the task of revealing the secret of their therapeutic value by systematically investigating them phytochemically.

Some of the recent works on cardiac active constituents are:

1. Cardenolides in the latex and leaves of seven *Asclepias* species and *Calotropis procera*\(^{53}\).
2. New Cardiac Glycoside from the leaves of *Digitalis lanata*\(^{54}\).
3. Cardiac Glycosides from the leaves of *Digitalis cariensis*\(^{55}\).
4. Chemical degradation of sarverogenin. Proof for the presence of the steroid carbon skeleton\(^{56}\).
5. Further Triterpenoids and \(^{13}\)C NMR spectra of oleanane derivative from *Phytolacca acinosa*\(^{57}\).
6. Effect of angiotension II on the antitumor activity and cardiotoxicity of doxorubicin\(^{58}\).
7. Pregananes and cardenolides from *Periploca sepium*\(^{59}\).
8. Preparation of amino sydnonimides cardiovascular agents\(^{60}\).
PROBLEM TAKEN AND WORK DONE:

The volume of danger signals that mankind has commenced to face in respect of his living habits, environment, quality of life has compelled him to peep into traditional medical lore, which stood the reveals of time and continued to shower its best for the benefit of mankind. An ethnic medical knowledge has anthropological background and a careful and deep look into it brings to the door front of common man the cheaper drug as has been advocated in Ayurveda and Siddha.

The author was fascinated by the recent report of use of cardiac glycoside from the bark, stem and roots of Digitalis purpurea for the treatment of heart failure, hypertension and because of earlier reports of presence of cardiac glycosides in some plants chosen by the author (i) Convallaria majalis Linn. and (ii) Urginea indica Roxb. Therefore it was thought worthwhile by the author to take up the challenging task of unrevealing the secret of their therapeutic value by systematically investigating them and his finding are summarised below:
(I) ISOLATION AND STUDY OF A NOVEL CARDIOGENIN (5-deoxy strophanthidin) FROM THE RHIZOMES OF CONVALLARIA MAJALIS LINN.

This chapter incorporates the details of isolation and structural elucidation of a novel cardiogenin (0.072%) molecular formula $\text{C}_{23}\text{H}_{32}\text{O}_{5}$, m.p. 235-237° and $M^+ = 388$ isolated by subjecting to column chromatography, the methanol soluble part of the concentrated 95% ethanolic extract of rhizomes Convallaria majalis Linn.

Various chemical degradation and colour reactions along with spectral studies (UV, IR, $^1$H NMR and Mass) established its structure as : 5-deoxy strophanthidin (I).
(II) ISOLATION AND STUDY OF A NOVEL CARDENOLIDE (4:5-Anhydro periplogenin 3-O-α-L-rhamnopyranosyl (1→5) O-β-D-xylofuranoside) FROM RHIZOMES OF CONVALARIA MAJALIS LINN.

This part deals with the isolation and structural elucidation of a novel cardenolide (0.086%), molecular formula C_{34}H_{50}O_{12}, m.p. 174-176° and M⁺ = 650 isolated from the ethyl acetate soluble part of the concentrated 95% ethanolic extract of rhizomes of Convallaria majalis Linn. Usual chemical degradations colour reactions and UV, IR, ¹H NMR and Mass spectral studies led to its identification as: 4:5-anhydroperiplogenin-3-O-α-L-rhamnopyranosyl (1→5) O-β-D-xylofuranoside (II).
(III) ISOLATION AND STUDY OF A NOVEL CARDIOGENIN (6-desacetoxy scillirosidin) FROM THE BULBS OF URGINEA INDICA Roxb.

The study of a novel cardiogenin (0.082%) molecular formula \( \text{C}_{24}\text{H}_{32}\text{O}_{5} \), m.p. 200-202\(^\circ\) and \( M^+ = 400 \), obtained by subjecting to column chromatography the methanol soluble part of the concentrated 95% ethanolic extract of the bulbs of Urginea indica Roxb. has been dealt in this chapter.

Various colour reactions, usual chemical degradation and spectral studies (UV, IR, \(^1\)H NMR and Mass) identified it as 6-desacetoxy scillirosidin (III).
(IV) ISOLATION AND STUDY OF A SCILLADIENOLIDE (4:5-dehydro-14β-hydroxy scilladienolide 3-O-β-D-glucopyranosyl (1→4) O-α-L-rhamnopyranoside) FROM THE BULBS OF URGINEA INDICA Roxb.

The study of a scilladienolide (0.084%), molecular formula C_{36}H_{52}O_{13}, m.p. 186-188° and M^+ = 692 obtained by subjecting to column chromatography the chloroform:ethyle acetate (7:4) soluble part of the concentrated 95% ethanolic extract of the bulbs of Urginea indica Roxb has been dealt in this chapter.

Various chemical degradations, colour reactions and UV, IR, ^1H NMR and Mass spectral studies, identified it as: 4:5-dehydro-14β-hydroxy scilladienolide 3-O-β-D-glucopyranosyl (1→4) O-α-L-rhamnopyranoside (IV).
REFERENCES


3. Wright S.E.; "Metabolism of cardiac glycosides"Black well oxford. 1960.


