The man who is ignorant, who has no faith, who is of doubting nature, perishes from the doubting soul there is neither this world, nor the world beyond, nor any happiness. We must have a positive basis of life, an unwavering faith, which stands the test of life.

-Bhagavathageetha.
## Chapter - I Drug Profile

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BACKGROUND OF PUBLISHED PAPERS:

India has an ancient heritage of traditional medicine. The materia medica of India provides a great deal of information on the Ayurveda, folklore practices and traditional aspects of therapeutically important natural products. It is very important to an Ayurvedic scholar to update the ancient therapeutic measures, which are given in classics and to find out new drugs and formulation without leaking the theoretical essence. So it is an inevitability to review the drugs and related literatures for the proper understanding of Trisutra Ayurveda i.e. Hetu, Linga, Aushadhagyanam, thereby for the betterment of both healthy and ill presents. Traditional systems of Indian medicine is unique but there is a common thread in its fundamental principle and practice. With the emerging worldwide interest in adopting and studying traditional systems and exploiting their potential based on different health care systems, the evaluation of the rich heritage of traditional medicine is essential. The government and the private sector are exploring all of the possibilities for the perfect evaluation of these systems in order to effectively adopt the therapeutic approaches available in original systems of medicine as well as to help in generating data to put these products on the national health program. The evaluation of these drugs is primarily based on phytochemical, pharmacological, and allied approaches including various instrumental techniques such as chromatography, microscopy, and others. *Solanum nigrum* was studied for many activities. These screening of the drug helps to understand the behavior of the drug in the body. In the context of holistic medicare the concept of therapeutic measures needs greater attention to be paid to the broader systems of environment and culture and their interconnections to understand the use of traditional therapies

*Solanum nigrum* was screened for antioxidant property. In one of the study it is found that it doesn’t possess the significant antioxidant activity. In the study the Methanolic extract was used for experiment and its radical scavenging potential was also evaluated and the assessment was done by Griess assay. In another study it is found that the extract of the plant contains calf thymus DNA and free radical generating system, which protects DNA against oxidative damage to its deoxyribose sugar moiety. The effect was depends on concentration of plant extract. It is observed that the hepato-
protective effect of the plant may be due to their ability to suppress the oxidative
degeneration of DNA in the tissue debries³.

*Solanum nigrum* was widely studied for cytotoxic and antitumor activity. It is
found that it has remarkable cytotoxic and apoptotic effect. *Solanum nigrum* glycoprotein
induces apoptosis and it is one of the chemotherapeutic agents⁴. 50% ethanol extract of
whole plant of *Solanum nigrum* was tested for cytoprotection against gentamycin-induced
cytotoxicity. The cytotoxicity was significantly inhibited as assessed by Trypan blue
exclusion assay. Extract also exhibited significant hydroxyl radical scavenging potential.
Thus, it suggests the probable mechanism of cytoprotection⁵. *Solanum nigrum*
glycoprotein shows a dose dependent radical scavenging activity on radicals⁶. This
glycoprotein caused a strong cytotoxic effect, rather than a radical scavenging effect.
Apoptosis, according to the apoptosis assay, increased as a result of treatment with
glycoprotein in a time-dependent manner. Consequently, this glycoprotein may induce
apoptosis through the inhibition of NF-kB activation, induced by oxidative stress in HT-
29 cells⁷.

The *Solanum nigrum* ethanol extract by proliferation assay shows the proliferative
capacity of MCF-7 cells was strongly suppressed. MTT assay and trypan blue exclusion
experiments showed a very close correlation between the *Solanum nigrum* extract
concentration and the surviving cell number. This extract was revealed to be potential
scavenger of hydroxyl radicals and DPPH radicals rather than superoxide anions. Thus
*Solanum nigrum* fruit extracts could be used as an antioxidant and cancer chemo-
preventive material⁷. Extract of *Solanum nigrum* showed cytotoxicity to *Salmonella*
typhimurium TA 100 in the absence of S9 mix. The toxicity of extracts from different
parts of plant, such as leaf, stem, immature fruit and mature fruit towards *Salmonella*
typhimurium TA 100 and human lymphocyte was also assayed. The immature fruit
extract exhibited strong cytotoxicity with dose dependent. It induced significant DNA
damage in human lymphocytes based on the comet assay. No mutagenisity was found to
TA98 or TA100 either with or without the S9 mixture⁸.

The isolation of *Solanum nigrum* glycoprotein, found that it was cytotoxic at low
concentration. With respect to cytotoxicity, it is found that SNL glycoprotein induces
apoptosis through modulation of PKCa and NF-κB activity in MCF-7 cells. Collectively,
the data demonstrate that this glycoprotein is a potential natural anticancer agent because of its ability to induce apoptosis in MCF-7 cells\textsuperscript{9}. The TPA-induced MCF-7 cells are the part of human breast cancer cell line without estrogen receptors. \textit{Solanum nigrum} glycoprotein might be one of the agents that blocks TPA-mediated signal responses in tumor cells\textsuperscript{10}. One attempt was made to identify carcinogens contribution in the food at high incidence of esophageal cancer in Transkei diet. Food collected from the gardens belonging to families in which the members had developed Esophageal cancer. The two groups was studied the one, which contain maize, beans and salt mixture and the second, contain full Transkei diet consisting of \textit{Solanum nigrum}. The second group develops severe liver lesions and epithelial-cell dysplasia of the esophagus. The group was also suffered from an increased incidence of tumors of various types. The same factor may also contribute the high incidence of esophageal and liver cancer occurring in the man in the Transkei\textsuperscript{11}.

One study was carried out by using mouse peritoneal macrophages and examined the mechanism by which \textit{Solanum nigrum} regulates NO production. It is found that there was a marked cooperative induction of NO production. Nitric oxide (NO) is an antitumor molecule produced in activated macrophages\textsuperscript{12}.

The use of leaves of \textit{Solanum nigrum} as antidiabetic agents was studied by using the oral glucose tolerance. It is found that there was no significant lowering in blood glucose levels by \textit{Solanum nigrum}\textsuperscript{7}. One study was carried out for estimation of tress elements in some antidiabetic medicinal plants using PIXE technique. It shows that the presence of the elements like K, Ca, Cr, Mn, Cu and Zn, in are responsible for potentiating insulin action\textsuperscript{4}. Not all the elements but \textit{Solanum nigrum} leaf contain Ca, P, and Fe. \textit{Solanum nigrum} also has Beta-carotene, rich source of riboflavin, nicotinic acid, and vitamin C. Higher values for vitamin C (20-40 mg./100 g.) have also been reported including protein, 5.9; fat, 1.0; minerals, 2.1; and carbohydrates, 8.9 g\textsuperscript{13}.

\textit{Solanum nigrum} was screened for CNS depressant action. The ethanol extract of fruit significantly prolong sleeping time, alteration in general behavior pattern, reduce exploratory behavior pattern, suppressed the aggressive behavior, affected locomotor activity, and reduced spontaneous motility, i.e. it possess potential CNS-depressant action\textsuperscript{14}. 
One of the study highlights to analyze the production of reactive oxygen species (ROS), lipid peroxidation and lypoxygenase activity. The relative increase in ROS production was higher in the susceptible clone H-8150 than in the resistance genotype. Lipid peroxidation increased only in the non-host *Solanum nigrum*. Increase in Lipid peroxidation in *Solanum nigrum* leaves coincides with enhances Lipoxygenase (LOX) activity. *Solanum nigrum* also has strong scavenging activity against lipid peroxyl radicals. Plasma lipoprotein levels (TG, TC and LDL) were significantly reduced. *Solanum nigrum* glycoprotein can be used as cholesterol lowering agent even at low concentration. With the aim of diversifying the lipids sources eaten by the African populations and those of Congo Brazzaville in particular, a physicochemical study of *Solanum nigrum* seeds was carried out. The dry matter content of the seeds is 94.22%. Average lipids content varies between 34.5 and 37.5% dry matter, proteins content is 17% dry matter and crude ash content averages 7.18% dry matter and the principal mineral element is Mg (180 mg/100g). The fatty acid compositions of *Solanum nigrum* seeds oil shows that it has 67.9% of linoleic acid, indicating its high unsaturation. Apart from linoleic acid, other prominent fatty acids were palmitic, stearic and oleic acids.

*Solanum nigrum* was studied for ulcer healing activity on acetic acid induced ulcer model. It showed concomitant attenuation of gastric secretory volume, acidity and pepsin secretion in ulcerated rat. Thus, offer antiulcer activity by blocking acid secretion through inhibition of H⁺K⁺ATPase and decrease of gastrin secretion. This might be due to antisecretory activity. The antiulcerogenic effects of the methanolic extract of *Solanum nigrum* berries (SBE) on aspirin induced ulceration in rats with respect to antioxidant status in the gastric mucosa have been investigated. The results indicate that the extract may exert its gastroprotective effect by a free radical scavenging action. The observations suggest that this extract may have considerable therapeutic potential in the treatment of gastric diseases. The drug was also studied for antinociceptive, anti-inflammatory and antipyretic effects of Chloroform extract in animal models. *Solanum nigrum* also perform the Antifungal activity.
CLASSICAL REVIEW:

Ayurveda the Science of Life deals with the health and longevity by preventive and curative measures. Dravyaguna is a specialized branch that deals with all the Karya Dravyas with its seven basic aspects like Dravya, Rasa, Guna, Veerya, Vipaka, Prabhava and Karma. The foundation of Ayurveda can be traced back over 6000 years, having divine origin. In fact Jeevaka, an ancient physician quoted that there is no plant available on the face of earth, which doesn’t have a medicinal value.

Initially Dravyaguna was not mentioned as a separate branch of Ayurveda but Raj Nighantu (17 AD), who first time mentioned it is also one of the main branches in Astang Ayurveda. Even-though all the treatises of Ayurveda elaborately described about the herbs, their properties and actions.

It is evident that Ayurveda is a science of life and most of the theories are based on the extraordinary observations and thus the description of drugs have been explained on the basis of several features like Rasa, Guna, Veerya, Vipaka, etc. So in this regard Charaka has explained the qualities of Vaidya, that one should have detailed knowledge of identification of drugs for perfect implementation in disease. There has been pointed indication that while establishing or advancing any theory or opinion, one should consider all the factors from all the angles and to the extent possible. Later the exact nature of the problem or Tatva is to be taken up for finding as solutions.

सर्वथा सर्व आलोच्य व्यासस्वभव अधिवित ।
अथ अध्यवसेत तत्वे च कार्य च तदन्त्यर्गम ।।

च. वि. 4/10

HISTORICAL REVIEW-

Description of Kakamachi is found in all the Ayurvedic literature. The drug is explained first time in Vedic Granthas. It was also widely used in Samhita period especially in the form of Shakdravya. It was used as Aushadhi Dravyas in various applications. Gadanigraha is the one who mentioned a special chapter in Rasayanadikara on Kakamachi.
VEDIC PERIOD-

The description of Kakamachi is explained first time in Vedic Granthas of Koushikasutra. It is described along with Bhrungaraj for the prevention of Keshadosha. In Keshava Paddhati the fruits were used for Keshavrudhi as Phalamani Bandhan. One reference was found as ‘Nitatni’. Sayanacharya gave the comment that ‘Nitatni’, means ‘Nyakprasaranasheela Oshadhihi’, which indicate, the drug like Kakamachi. The reference of Nitatni is related with Keshabramhini and Balya and is supposed to be a plant, which spreads below the ground, having synonyms Devi and Chupunika. There is no evidence found where Nitatni can be consider as Kakamachi.

SAMHITA PERIOD-

All Samhita have described Kakakmachi for Shaka Dravya as well as Oushadha Dravya. It is observed that the drug is very popular in those days, which was studied well and used widely in the therapeutics and in dietary supplement. They have explained the drug in the form of therapeutical application as well as contraindicated with some combination and application.

Charaka Samhita: Charaka has explained the drug in Tikta Skandha and as a Shaka Dravya. Charaka has widely used Kakamachi as a Shaka Dravya in Shushkarsha, in Vataja Kasa, Urustambha and in Vatarakta. As an Oushadhi Dravya, he has explained Kakamachi in Aragwadadi Lepa for Kushtha and as a Patra Kalka in Kushtha. It is one of the ingredients in a Shothahara lepa, Pradeha in Veesarpa and in Mahanil Tail. He mentioned many contraindications to the use of Kakamachi. Some of like that; it becomes Sanyoga Viruddha with Matsya Siddha Tai. If it used regularly in more quantity and in Ajeerna Awastha, it will become the cause for Kustha. It is contraindicated while using Yogaraja Kalp.

Susruta Samhita: Like Charaka, Susruta also explained the drug in the same fashion. He mentioned the drug in a Shaka Varga and also explained it in a Suarasadi Gana. He has given its contraindication that it should not be taken with Pippali and Mareecha and also with Guda.

Astang Hridaya: In Astang Hridaya there are vivid references of Kakamachi are found.
Bhavaprakasha Samhita: In Bhavaprakash there are many references of Kakamachi found either single or in combination with other ingredients.

Gadanigraha: In Gadanigraha, Kakamachi is found in many formulations. He has mentioned a separate Rasayana chapter on Kakamachi.

MEDIEVAL PERIOD-

Nighantu -

In Nighantu period individual drugs were specially highlighted. Depending on the ideology of a Nighantukara they have described the drug in different Ganas or Vargas. These Nighantus are considered as a thesaurus of the single drugs and have got separate importance in parallel to the other eight branches of Astang Ayurveda. Raj Nighantu, the one who even considers Dravyaguna is a branch of Astang Ayurveda. According to different Nighantukara the vivid descriptions of Kakamachi are as follows-

Astang Nighantu (8th Century)- Astanga Nighantu has described the drug and has also given its many synonyms.

Dhanvantari Nighantu (10th Century AD)- Dhanvantari Nighantu has described the drug in Karaveeradi Varga. He has described its synonyms and properties.

Amar Kosha (11th Century AD)- He has described the drug under Vanoushadhi Varga in second Kand. He has also mentioned its synonyms and its interpretations.

Chakradatta (11th Century AD)- He has mentioned the drug in various preparations as well as a single drug therapy.

Shodhal Nighantu (12th Century AD)- He has mentioned the drug under Karaveeradi Varga by mentioning its synonyms and properties.

Madanpal Nighantu (14th Century AD)- He has mentioned the properties of the drug and its synonyms.

Kaiyadeva Nighantu (15th Century AD)- He has mentioned Kakamachi in Aushadhi Varga and given different synonyms and properties.

Bhavaprakasha Nighantu (16th Century AD)- Bhavaprakash has mentioned the drug in Guduchyadi Varga. He has also given its synonyms and properties.

Raj Nighantu (17th Century AD)- Raj Nighantu has given a wide description of Kakamachi. He has give eighteen synonyms and properties of Kakamachi. He describes the drug under Shatavhadi Varga.
Shaligram Nighantu (19th Century AD) - He has mentioned the drug and given its properties along with its action on Dosha.\(^1\)

Nighantu Ratnakara (20th Century AD) - He has mentioned the drug under Guduchyadi Varga and described its synonyms and properties.

Abhinava Nighantu (19th Century AD) - He has mentioned the synonyms and properties of the drug. He has also given different Amayik Prayoga and Vernacular names of Kakamachi.\(^2\)

Priya Nighantu (20th Century AD) - He has mentioned the drug under Shatapushpadi Varga and described its properties.\(^3\)

Rasasastriya Granthas

Kakamachi is extensively used in all Rasasastriya Granthas. In almost all the Rasagrantha Kakamachi is used either in Bhavana Dravya or as an ingredient in the formulation. It is the drug used for Parada Bandhanas and having the position in different Ganas like Kakarashtak, etc. Some of the Granthas like:

Rasaratnasamuchchaya: The reference of Kakamachi is found in various places in Rasaratnasamuchchaya including its contraindication at the time of Rasasevana. Its description is mostly found in the form of Bhavana Dravya or as one of the ingredient in the formulation. He has described the drug under the Vishghna Gana. He has also described it as one of the Rasa Bhavanadi Moolini Dravyas. Rasaratnasamuchchayakar has described it in the preparation like: Lokanath Gutika, Hrudayarnava Rasa, Vanhijwala Vati Rasa, Vadavanala Gutika, Vajreshwar Rasa, Sparshavatari Tailam, Sarvaroganashana Rasayana, Vishakalpa and Kilasahara Yoga.

Rasatarangini: In this Grantha, we can find the use of Kakamachi in various manners. He has described the drug under Rasasya Niyamak Gana, Parada Marak Gana, Kakarashtak, Abhvak Maran Dravya, Abhraka Marana Gana. The Grantha has described the drug in Vamana Hara Yoga, as a Kushtahara.

Basavarajeeyam: In this Grantha we can find the use of Kakamachi in various preparations like Kalakutarasa, Rasarajendra Rasa, Agnikumar Rasa, Prabhavati Gutrika, Rudraparpati, Grahanyankusha Rasa, Hrudayarnava Rasa, Someshwara Rasa, etc. It has described the drug as Jwarapathyakara Shaka.
MODERN PERIOD

After 16th Century, there is heavy research carried out on medicinal plants in different dimensions of science. There are many Ayurvedic textbooks and reference books of medicinal plants, which described Kakamachi in details. The list of such books is very long and cannot be concise due to vast literature. But some of the specific books whose literature can be considered as worthwhile are-

**Dravyaguna Vignyana:** The author Acharya Priyavat Sharma has mentioned the drug elaborately in his different volumes. He has highlighted the synonyms, properties, indication, therapeutic properties, formulations and in brief about its morphology and habitat. He has ruled out its controversy and highlighted the drug from its existence in Vedic Period. He has also given its photographs.

**Dravyaguna Vignyana:** The author, V. M. Gogate has mentioned the drug and its synonyms, properties, indications, therapeutic properties, formulations and in brief about its morphology and habitat.

**Nighantu Adarsha:** The author, Bapalal Vaidya has mentioned the drug elaborately in Kantakaryadi Varga. He has highlighted the synonyms, properties, indications, therapeutic properties, formulations and in brief about its morphology and habitat. He has also mentioned the therapeutics in different texts with references.

**Sandigdha Nirnaya Vanoushadha Sastra:** In this book the author has mentioned the classical references, indications and uses of Kakamachi.

**Vanoushadhi Chandrodaya:** In this book, the author has described the synonyms with vernacular names along with the total description of the plant. The author has also mentioned the Guna, Dosha and Prabhava of Kakamachi. He has specially mentioned the opinion of Unani and given presence of chemical constitutions.

**The Indian Materia Medica:** The author has described the synonyms, vernacular names, constituents and action of the drug. He has also explained the therapeutic uses of the medicine and its side effects.

**Database on Medicinal Plants used in Ayurveda:** It is published by CCRAS, having wide routine description like synonyms, vernacular names, action, uses, etc along with pharmacognosy, pharmacological activities, cultivation, etc.
Indian Medicinal Plants: It is one of the most referred books in India for medicinal plants. In it a wide variety of vernacular names, description of plant with sketch diagram, and its different therapeutic uses are explained.

Indian Medicinal Plants: A Compendium of 500 species- Published by Arya Vaidya Shala, Kottakkal, is one of the most referred book for Ayurvedic medicinal plants. The wide variety of Ayurvedic herbs with references, vernacular names, description of plant with sketch diagram, and different therapeutic uses are mentioned in it.

CONTROVERSY-
As the literature view reveals there are no controversies regarding Kakamachi. Being a Shaka Dravya it is very much known to common being and Vaidya community. Many a times, this drug is confused with Kakajangha, Kakanasa, Kakanasika, etc. Hence it may be considered that all are from same morphological or therapeutic Varga or are considered as having common origin of their synonyms that are related with crow. Some synonyms like Vayasi, Kakanasika are also mentioned for Kakajangha and Kakanasa along with Kakamachi. But it is very clear that Kakamachi is very common plant used as Shaka Dravya and deeply rooted in the society for its various needs. Charaka, Susruta etc have never mentioned its synonyms and but given its clear-cut references. The drug named as Nitatni also raised the controversy. But Sayanacharya clears the point by mentioning its resembles with Kakamachi. According to Ayurvedic Pharmacopoeial committee the drug is very clear for identity and was denoted as Solanum nigrum.

CLASSIFICATION-
Kakamachi has been explained by different Acharyas under various Varga or Skandha. The classification mainly explains about the type and the style of presentation of their treatise.
Table No. 1.1

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<tr>
<th>S No.</th>
<th>Varga / Gana / Skandha</th>
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<td>Ch. Su. 27/90</td>
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<td>2</td>
<td>Tikta Skandha</td>
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<td>3</td>
<td>Surasadi Gana</td>
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<td>4</td>
<td>Karaveeradhi Varga</td>
<td>Dhanvantari Nighantu -19</td>
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<td>5</td>
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<td>Kaiyadeva Nighantu -71</td>
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<td>Rasa Bhavanadi Moolini Dravya</td>
<td>Rasaratnasamuchchaya 11/58</td>
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<td>Abhraka Marana Gana</td>
<td>Rasatarangini 10/56</td>
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SYNONYMS-

Kakamachi has been explained by different synonyms to exhibit its original morphological or pharmacological properties especially to identify the drug. The every next new treatise added some more names to establish the identity of the drug. It is found that there are some synonyms, which sometimes confuse the original nature of the drug. These synonyms are like:
Table No. 1.2

<table>
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<tr>
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Interpretation of Synonyms:

1. Katwi - कट्यते कटुरसतया खाधये अनुभूयते वा।
   The word Katwi refers to the Katu Rasa of the fruit of the plant.

2. Katuphala - कटफलम् यस्य।
   The fruit of the drug have Katurasa.


4. Rasayanavara - Performing the effect of Rasayana Karma or consider as the best in Rasayana karma.

5. Sarvatikta - This refers to the bitter test of the Kakamachi or whole plant should have Tikta Rasa except fruit as it mentioned separately.

6. Swadupaka - or Swadupakaphala - स्वादुपाककपम् यस्य।
   The Vipaka of the Phala is Madhura in nature so called as Swadupaka or Swadupakaphala.

7. Vidravini - पलायनम् ईत्यमर। निन्दा क्षरणम।
   The word Vidravana refers to the driving or scaring away the deranged Dosha. It also refers to the Vrushya property of the drug which helpful in sexually satisfaction of the partner by Ksharana of Shukra. The word Ksharanam also refers to the winning phenomenon in the sex indulges as it has Vrushya property. The drug has Anushna Veerya and Katu Rasa, which is responsible for melting (Vidravan) of the excessive Kapha in the body. The word Vidravana is also considered as Palayanam, which reflects on, the original nature of Kaka (crow).

8. Kushthanashini - or Kushthaghni - कृष्ठनाशयतीत।
   The word denotes the action of a drug on skin disorders or all types of Kushthaveekara. The drug has Tikta Rasa and Tridosaghna property so; it must have action on Kushtha Roga. It is also found that the many formulations of Kakamachi used on skin disorders.
9. Tiktiika- This word refers to the bitter test of the Kakamachi or whole plant should have Tikta Rasa.

10. Bahutikta- बहुतिक्तोर्सी यस्या ।

   The drug has excessive bitterness in the test.

11. Rasayani- Performing the effect of Rasayana Karma or consider as the best in Rasayana karma.

12. Gudaphala- गुड ईव मधुरम् फलम् यस्या ।

   At the stage of ripening the test of the fruit is sweet in nature. In the villages the children regularly eat it and which tastes like Guda (Jiggery).

13. Shakamata- The drug is highly used as a Shaka dravya as well as explained in Shakavarga. This may be the reason to denote it as Shakamata.

14. Kaka- This may be the ‘Upama’ given to the plant to denote its behavioural or morphological character.

15. Kakamachi-

   काकान मनन्यते अर्धयति फलदानेनिनिति ।
   क्षुद्वृक्तवृष्टिशेष गुडकामाईः ईविति भाषा तत्त्वयं: वायवसी ।।

   This indicates that the crows are very fond of the plant, which attracts them. The plant is also considered as inferior or Kshudra (small / inferior) species of Vruksha. It is also known as Gudakamai in general language and it has Vayasi as synonym.

   काकवन्यचति क्वःन सम्प्रचते फलं यस्य: ।

   This indicates the plant whose fruits are black in color.

16. Dhwankshamachi-

   ध्वांक्षान काकान मनन्यते पूज्यति फलदानेनिनिति ।

   Dhwanksha refers as the synonym of Kaka (Crow) having the same meaning as Kakamachi. The word Dhwanksh also denotes a meaning of Beggar, this may be the reason why the plant is considered as Kshudra Vrukshavishesha. The word Dhwanksha refers to an impudent (Non polite, rough) fellow, which highlights the drug is not a casual to utilize as regular drug and indicate the harsh effect if not tackled well. The drug many a times described under Viruddha Anna category and explained guidelines to be followed while utilizing the drug either as a food or medicine or in combination with other drug.
17. Kakavha- This also refers to the word Kaka as crow and indicates to Kakamachi.

18. Vayasi-

The drug is liked by the Kaka (crow).

19. Vayasavha-

The crows are fond of this drug and hence it seems that the drug is attracting or calling the crows towards it.

20. Bahuphala-

It indicates that the plant has many fruits.

21. Guchchhaphala-

The fruits are growing in groups or in bunch called as Guchchhaphala.

22. Kakamata-

The plant nourishes the crows, like mother and its fruits are very much liked by the crows.

23. Sundari- It looks good and attractive.

24. Matsyakshi-

The petels of the flower are seems as the eyes of the fish.

25. Kakini-

The actual meaning of the word indicates the quarter of the Pana or measure. As such there is no relation can be established with this meaning and the plant. The synonym may be the Apabhrinsha of words related with Kaka (crow).

26. Kakasavha-

This is the same interpretation like Vayasavha where the word Kaka is the synonyms of Vayasa i.e. crow. This again seems to invite crow to the plant due to its affinity.

27. Kamata and Kamachi - This may be due to the series of the word related with Kak, which interpret the relation between crow and the plant.
28. Jaghanephala— जघनेफलम यस्यः।
जघने अधोभागे फलतिति। जघनेवा मध्यभागे फलमस्यः।

The fruits are situated in the mid portion of the branch and not exactly to the peripheral portion.

**RASAPANCHAKA—**

Kakamachi is one of the very popular plants and described in many texts. Many of the text attributed a common opinion about the Rasapanchaka of Kakamachi, only few having different opinion. Some texts described Rasapanchaka for the different part of plant like fruit. The vivid opinions about Rasapanchaka of Kakamachi are as follows—

Table No. 1.3

<table>
<thead>
<tr>
<th>S. N</th>
<th>Grantha / Nighantu</th>
<th>Rasa</th>
<th>Veerya</th>
<th>Vipaka</th>
<th>Guna</th>
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<tbody>
<tr>
<td>1</td>
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<td>Katu and Madhura (Phala)</td>
<td>Snigdha, Ushna, Laghu</td>
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<td>Snigdha, Ushna</td>
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</table>
Overall Kakamachi has-

- **Rasa-** Tikta, Katu
- **Guna-** Snigdha, Ushna, Sara, Laghu
- **Veerya-** Ushna
- **Vipaka-** Katu (Fruit-Swadu)
- **Doshaghnata-** Tridoshaghna


**Action and Uses** - The plant is bitter, acrid, emollient, mildly thermogenic, antiseptic, anti-inflammatory, expectorant, digestive, laxative, diuretic, cardiotonic, depurative, diaphoretic, febrifuge, hydragogue, rejuvenating, sedative, alterant and tonic. It is useful in rheumatic affections, inflammatory swelling, cough, asthma, bronchitis, wound, ulcers, flatulent, dyspepsia, hepatomegaly, otolgia, hiccough, nasal catarrh, ophthalmic disorder, vomiting, cardiac disorders, leprosy, skin diseases, fever, spleenomegaly, haemorrhoids, hoarseness, nephropathy, dropsy, gonorrhoea and general debility. A decoction of plant depresses the central nervous system and reflexes of the spinal cord and has influence on cardiac activity and in regulation of blood pressure. Leaves are used as poultice for rheumatic and gouty joints and skin diseases. A decoction of berries and flowers is useful in cough, erysipelas, rat bite, bronchitis, pulmonary tuberculosis, fever, diarrhea, ophthalmpathy and hydrophobia. Seeds are useful in giddiness, inflammation and skin diseases. The root bark is useful in diseases of ear, eye, nose and hepatitis. The leaves and berries are especially important as a cure for gastric ulcer.

**Pharmacological Activities** - Anti-inflammatory, hepatoprotective, antiseptic, narcotic, antispasmodic, antibacterial, antimicrobial, CNS depressant, antiulcer, cardiac depressant, immunomodulator.

**Therapeutic Evaluation** - The use of *S. nigrum* as stock for tomatoes to counteract the heat in North India has been suggested. The herb has antiseptic and Anti-dysenteric properties and is given internally for cardalgia and gripe. An infusion of the plant is used as an enema in infants having abdominal upsets. It is a household remedy for anthrax pustules and is applied locally. The plant is also credited with emollient, diuretic and laxative properties and its decoction is regarded as an antispasmodic and narcotic. Freshly prepared extract of the plant is effective in the treatment of cirrhosis of the liver, and also serves as an antidote for opium poisoning. An alcoholic extract of leaves is active against *Staphylococcus aureus* and *Escherichia coli*. Infusion or decoctions of the plant after transient stimulation, depress the central nervous system and the reflexes of the spinal cord. Small doses increase, and large doses decrease, cardiac activity; reduction in blood pressure is also evident; in the isolated rabbit ear, vasodilatation has been observed. Decoction of the plant may be used for the treatment of ascites in dogs. Leaves are used in treatment of scrofulous dyscrasias, and
are said to produce diaphoresis when in overdose; they also cause nausea, purging and nervous disturbances. In China, leaves are applied to wound and sores. The juice of fresh leaves is reported to produce dilation of the pupil. In the Philippines, the pounded leaves are rubbed on de-pigmented areas of the body for restoring the pigment.

A compound herbo-mineral proprietary medicine, containing *S. nigrum* as one of the constituent, was found efficacious in treatment of chronic hepatitis, infective hepatitis and cirrhosis of liver. Leaves and tender shoots of *S. nigrum* are boiled as spinach and eaten in many parts of India, especially by patients suffering from dropsy. Ripe fruits are used in pies and preserves; they are sometimes used as substitute for raisins in plum puddings. Fruits make a delightful jam. Berries are considered to possess tonic, diuretic and cathartic properties and are useful in anasarca and heart diseases. They are the domestic remedy for fever, diarrhea, ulcers and eye troubles. Aqueous extract of the ripe fruit inhibit choline esterase activity of human plasma.

**Contraindications**

Kakamachi has widely been used both Ahara Dravya and Oushadha Dravya. In specific conditions either in diet or in Oushadha Sevanakala, it is supposed to be considered as incompatible drug. In the text, there is time-to-time explanation about the administration of the drug. Charaka interpreted the drug as a Sanyoga Viruddha and having Sadya Maraka effect, if it is taken with Matsyasiddha Tail and Pippali. He also indicated that the drug should not be taken always in more quantity and in Ajeernavastha. Charaka has also contraindicated Kakamachi while prescribing Yogaraja Kalpa. Like Charaka, Susruta also contraindicated Kakamachi especially with Pippali, Mareecha and Guda, as it becomes incompatible. Later on Gadanigraha also objected intake of Kakamachi while administering Vajraka Gutika.

**Toxic Effects**

Green unripe fruits contain glycol-alkaloids and their consumption in large quantity may cause toxic hazards, even death, to human beings as well as livestock. It is also reported that 2-3 children have died due to consumption of ripped fruit of this plant.
Part Used-

There is a common concept in Ayurveda for selecting a specific part of a drug as a single or in formulation, if there is no indication of said useful part\textsuperscript{113}. As per this aspect, Kakamachi is having thin roots so that its whole plant is considered as a useful part for administration\textsuperscript{114}. But in some indications or formulations Samhitakara has given specific useful part like Patra in Aragwadhadi Lepa\textsuperscript{115}, Patra Kalka Lepa in Kushtha\textsuperscript{116}, Pushpa in Mahanil Tailam\textsuperscript{117}, Root and Twak in Nidranasha\textsuperscript{118}, etc. It is also found that the whole plant and in fruits are very useful\textsuperscript{119}.

Formulations-

Kakamachi is used many times as an ingredient in many of the formulations in different text.

Table No. 1.4 Formulations of Kakamachi

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<th>S. No.</th>
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<td>G N Ghrutadhikara / 86</td>
</tr>
<tr>
<td>10</td>
<td>Mahneel Tail</td>
<td>G N Tailadhikara / 480</td>
</tr>
<tr>
<td>11</td>
<td>Dwi-Panchamooladya Tailam</td>
<td>G N Tailadhikara / 489</td>
</tr>
<tr>
<td>12</td>
<td>Dwitiya Mahaneel tailam</td>
<td>G N Tailadhikara / 516</td>
</tr>
<tr>
<td>13</td>
<td>Khadeeradi Vatika</td>
<td>G N Gutikadhikara / 122</td>
</tr>
<tr>
<td>14</td>
<td>Vajrak Gutika</td>
<td>G N Gutikadhikara / 245</td>
</tr>
<tr>
<td>15</td>
<td>Triphaladi Tailam</td>
<td>G N Medorogadhikara / 23</td>
</tr>
<tr>
<td>16</td>
<td>Haridradya Udvartana</td>
<td>G N Kustharogadhikara / 129</td>
</tr>
<tr>
<td>17</td>
<td>Chaturangulparnyadi Lepam</td>
<td>G N Kustharogadhikara / 174</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
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<td>---</td>
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</tr>
<tr>
<td>18</td>
<td>Vayasyadi Lepam</td>
<td>G N Kustharogadhikara / 243</td>
</tr>
<tr>
<td>19</td>
<td>Karna Guthak Nirharana Yoga</td>
<td>G N Karnarogadhikara / 67</td>
</tr>
<tr>
<td>20</td>
<td>Kakamachi Dhoop</td>
<td>G N Netrarogadhikara / 384</td>
</tr>
<tr>
<td>21</td>
<td>Kapitthadi Lepam</td>
<td>G N Balarogadhikara / 51</td>
</tr>
<tr>
<td>22</td>
<td>Vishahara Ghrut</td>
<td>G N Garavisha chikitsa / 10</td>
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<tr>
<td>23</td>
<td>Kakamachi Kalpa</td>
<td>G N Rasayana Tantra</td>
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<td>24</td>
<td>Hrudayarnava Rasa</td>
<td>YR</td>
</tr>
<tr>
<td>25</td>
<td>Gunja Garbha Rasa</td>
<td>YR</td>
</tr>
<tr>
<td>26</td>
<td>Dantashoola Nashaka Yoga</td>
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<td>27</td>
<td>Mahavishagarbha Taila</td>
<td>YR</td>
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<td>28</td>
<td>Kalakuta Rasa</td>
<td>Basavarajeeyam 1st Vol/2</td>
</tr>
<tr>
<td>29</td>
<td>Rasarajendra Rasa</td>
<td>Basavarajeeyam 1st Vol/2</td>
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<td>30</td>
<td>Agnikumara Rasa</td>
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<tr>
<td>31</td>
<td>Prabhavati Gutika</td>
<td>Basavarajeeyam 1st Vol/2</td>
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<td>32</td>
<td>Rudra Parpati</td>
<td>Basavarajeeyam 1st Vol/8</td>
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<tr>
<td>33</td>
<td>Grahanyankusha Rasa</td>
<td>Basavarajeeyam 1st Vol/10</td>
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<td>34</td>
<td>Nikruntaka Rasa</td>
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<td>35</td>
<td>Someshwara Rasa</td>
<td>Basavarajeeyam 2nd Vol/13</td>
</tr>
<tr>
<td>36</td>
<td>Shankar Vati</td>
<td>BR 33/52</td>
</tr>
<tr>
<td>37</td>
<td>Vishweshwari Rasa</td>
<td>BR 55/35</td>
</tr>
<tr>
<td>38</td>
<td>Bhruhat Lokanatha Rasa</td>
<td>BR 41/68</td>
</tr>
<tr>
<td>39</td>
<td>Rasa Parpati</td>
<td>BR 8/403</td>
</tr>
<tr>
<td>40</td>
<td>Sarivadi Vati</td>
<td>BR 62/72</td>
</tr>
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<td>41</td>
<td>Siddhaphala Paneeya Vatika</td>
<td>BR 5/666</td>
</tr>
<tr>
<td>42</td>
<td>Swachehhandanayaka Rasa</td>
<td>BR 5/805</td>
</tr>
<tr>
<td>43</td>
<td>Bruhad Vishamajwarantaka Rasa</td>
<td>BR 5/1157</td>
</tr>
<tr>
<td>44</td>
<td>Bruhad Dvitiya Sarvajwarahara Loham</td>
<td>BR 5/1183</td>
</tr>
</tbody>
</table>
Nutritive Values of Kakamachi

Analysis of leaves gave the following values (in 100 gm. Edible material): moisture, 82.1; protein, 5.9; fat, 1.0; minerals, 2.1; and carbohydrates, 8.9 g.; Ca, 410; P, 70; and Fe, 20.5 mg./100 g. Leaf is a rich source of riboflavin; the values for various vitamins present in the leaf are (in 100 g. edible material): riboflavin, 0.59; nicotinic acid, 0.92; and vitamin C, 11.0 mg. Leaves contain Beta-carotene (0.74 mg./100 g. material); Alpha-carotene content is negligible. Citric acid is present to the extent of 5 per cent. A flavokinase (opt. PH 8-6; opt. Temp. 40-450) is present in leaves. Fruits contain glucose and fructose (15-20%), vitamin C and Beta-carotene. Green unripe fruits, however, contain glycol-alkaloids and their eating is a toxic hazard to human beings as well as livestock. Ripe fruit contains very little alkaloids and can be consumed without ill-effects. Seeds, forming 9.5 per cent of the weight of the fresh fruit, contain 17.5 per cent protein on dry weight basis. They yield a greenish yellow oil (21.5%) with the following physical and chemical constants: sp. gr.30, 0.9198; n25, 1.4712; acid val., 11.62; sap. val., 184.0; acet. val., 25.7; iod. val. (Hanus), 123.2; Hahner val., 92.9; R.M. val., 0.66; and unsapon. matter. 1.4%. The component fatty acids of the oil are: Linoleic, 46.63; oleic, 49.73; palmitic, 1.76; and stearic, 1.88%. The unsaponifiable matter contains sitostanol.

Immature green fruit of the plant contains four steroidal glycol-alkaloids, viz. solamargine, solasonine and Alpha and Beta-solanigrine; all of them yield solasodine as the aglycon. It also contains the steroidal genine, tigogenine (m.p.,206-070). Solamargine and solasonine are also present in leaves. The total alkaloids content of fruit and leaves are respectively 0.101 and 0.431 per cent.

Description of Solanum nigrum Linn.
SOLANUM Linn. (Solanaceae)

A large genus of herbs, shrubs and rare trees are found throughout the temperate and tropical parts of the world. The genus is economically very important, as several species are sources of food, fodder and drugs. Some varieties are grown in gardens for ornament.
VERNACULAR NAMES

- **Africaans**- Galbessie, Nagskal, Nagskade, Nastergal;
- **Arabic**- Ambussalap, Enabeddir;
- **Assam**- Pichkati;
- **Bengal**- Gurkamai, Kakmachi, Mako, Tuldun;
- **Betsimisaraka**- Anantsatria;
- **Bicol**- Cuti, Lubilubi;
- **Bombay**- Ghati, Kamuni, Mako;
- **Brazil**- Carachichu, Erva moira;
- **Catalan**- Morella negra, Morella vera;
- **Chinese**- Long K’oui, Lung K’uei, T’ien Kuin Tse, Tien P’ao Tse;
- **Cutch**- Kamperu;
- **Danish**- Natskygge, Svineurt;
- **Dutch**- Swarte nagtschade;
- **English**- Black Nightshade, Common Nightshade, Garden Nightshade, Hound’s Berry, Morelle, Petty Morel;
- **French**- Bonbon noir, Creuzot, Creve-chien, Herbe a la gale, Harbe aux magicians, Herbe maure, Herbe more, Morelle, Morelle commune, Morelle de l’île de France, Morelle des jaedins, Morelle molle, Morelle noire, Morette, Mourette, Raisin de loup;
- **German**- Alpkraut, Berstelbeere, Garten Nachtschatten, Schwarzer Nachtschatten, Schwarze Nieswurz, Saurkraut;
- **Greek**- Strychnose, Sychnose;
- **Guiana**- Alaman, Laman;
- **Gujerati**- Piludi;
- **Hasada**- Burudian;
- **Hindi**- Gurkamai, Kabaiya, Makoi;
- **Hova**- Amelo, Anamafaitra;
- **Italian**- Ballerina, Morella, Soleno, Soletro;
- **Languedoc**- Crebo chin;
- **La Réunion**- Brede martin, Brede morelle;
- **Loralai**- Karezzi;
- **Madagascar**- Anamamy, Hange;
- **Malay**- Trong Parachicht;
- **Malinke**- Bassia bene;
- **Malta**- Black Nightshade, Ballerina, morella, Gheneb-id-dib, Tuffieh-tas-serp;
- **Marathi**- Ghati, Kakamachi, Kamoni, Laghukavali, mako;
- **Mexican**- Tohonechichi;
- **Naguri**- Burhidian;
- **New Zealand**- Poroporo. Raupeti;
- **Persian**- Rubahtareek;
- **Philippines**- Hierba Mora;
- **Polish**- Psinki Zele;
- **Portuguese**- Herva moura, Solano;
- **Punjab**- kachmach, Kambei, Kwansaf, mako. Riaungi;
- **Roumanian**- Lesnicioara, Umbra noptii;
- **Sind**- Kanperun;
- **Sinhalese**- Kalukanweriya, Kalukungwareiya, Tibbatu;
- **Spanish**- Solano negro. Solano officinal, Yerba mora;
- **Swedish**- Hanslatagrael;
- **Tagalog**- Camacamatisan, Conty, Cunti, Gamagamatisan, Lubilub, Onti;
- **Tamil**- Manattakkali;
- **Telugu**- Gajuchattu, Kachi, Kakamachi, Kamanchi, Kanchipundu, Kasaku;
- **Urdu**- Makoya;
- **Visayan**- Bolagtab, Hulablub, Lagparum;
- **Xosa**- Seshoa-behloko, umSobo, umSobosobo;
- **Zulu**- Umsobo.
MORPHOLOGY-

A variable annual; stem erect, glabrous or more or less pubescent and much divaricately branched. Leaves numerous, 2.5-9 by 2-5cm., ovate-lanceolate, sub-acute or acuminate, glabrous. thin. entire sinuate toothed, tapering into the petiole; petioles 2 cm. Long. Flowers small, in extra-axillary subumbellate 3-8-flowered cymes; peduncles 6-20 mm. long, slender; pedicels 6-10 mm. long, very slender. Calyx 3 mm long, glabrous or nearly so; lobes 5, oblong, obtuse, 1.25 mm. Long, not enlarged in fruit. Corolla 4-8 mm. long, divided more than ½-way down into 5 oblong sub-acute lobes. Filaments short, flattened, hairy at the base; anthers 2.5 mm. long, yellow. oblong, obtuse, notched at the apex. Ovary globose, glabrous; style cylindric, hairy. Berry 6-mm. diameters, globose, usually purplish black, but sometimes red or yellow, smooth shine. Seeds discoid, 1.5 mm. diameter, minutely pitted, yellow.¹²¹ (Figure No. 1.1)

GEOGRAPHICAL DISTRIBUTION-

Throughout India, Ceylon- all temperate and tropical regions of the world ¹²¹

SUBSTITUTES AND ADULTERATION

There is no reference found of any substitute of Kakamachi in any text of Ayurveda. As Kakamachi is available abundantly as a weed form so there is no possibility for adulteration in commercial market.

PHYTOCHEMISTRY OF SOLANUM NIGRUM- ¹²²

Table No. 1.5: Phytochemical evaluation of Solanum nigrum.
Figure 1.1- Solanum nigrum
<table>
<thead>
<tr>
<th>No.</th>
<th>Entry Name</th>
<th>Source / Synthesis</th>
<th>Other Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Solanum Alkaloid IV</td>
<td>Isolated from epigeal parts</td>
<td>Co-occurs with Solasonine, Solamergine &amp; B-Solamergine</td>
</tr>
<tr>
<td>2.</td>
<td>Alkaloid SN-c</td>
<td>Alkaloid from the berries</td>
<td>-</td>
</tr>
<tr>
<td>3.</td>
<td>Alkaloid SN-f</td>
<td>Alkaloid from the berries</td>
<td>-</td>
</tr>
<tr>
<td>4.</td>
<td>27-Carboxilic acid</td>
<td>Alkaloid from the berries</td>
<td>-</td>
</tr>
<tr>
<td>5.</td>
<td>Uttroside B</td>
<td>Solanum nigrum</td>
<td>-</td>
</tr>
<tr>
<td>6.</td>
<td>Uttroside A</td>
<td>Solanum nigrum</td>
<td>-</td>
</tr>
<tr>
<td>7.</td>
<td>2&quot;-O-α-L-Rhamnopyranosyl</td>
<td>Isolated from Solanum nigrum</td>
<td>-</td>
</tr>
<tr>
<td>8.</td>
<td>2&quot;-O-α-L-Rhamnopyranosyl, 6&quot;-O-β-D-glucopyranosyl</td>
<td>Solanum nigrum</td>
<td>-</td>
</tr>
<tr>
<td>9.</td>
<td>β – Solanigrine</td>
<td>Solanum nigrum</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>α – Solanigrine</td>
<td>Solanum nigrum</td>
<td>-</td>
</tr>
<tr>
<td>11.</td>
<td>12-β-Hydroxy, 23-acetoxy</td>
<td>Alkaloid</td>
<td>-</td>
</tr>
<tr>
<td>12.</td>
<td>Alkaloid SN-e</td>
<td>Alkaloid from the berries</td>
<td>-</td>
</tr>
<tr>
<td>13.</td>
<td>Uttronin A</td>
<td>Constituent of Solanum nigrum</td>
<td>-</td>
</tr>
<tr>
<td>14.</td>
<td>Uttronin B</td>
<td>Constituent of Solanum nigrum</td>
<td>-</td>
</tr>
</tbody>
</table>
CHEMICAL CONSTITUENTS

Table No. 1.6: Chemical constitutions of *Solamum nigrum*

<table>
<thead>
<tr>
<th>No</th>
<th>Entry Name</th>
<th>Molecular Formula</th>
<th>Molecular Wt.</th>
<th>Physical Description</th>
<th>Melting Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.</td>
<td>Alkaloid SN-f</td>
<td>C45H73N017</td>
<td>900.068</td>
<td>Amorphous Powder</td>
<td>-</td>
</tr>
<tr>
<td>3.</td>
<td>27-Carboxilic acid</td>
<td>C27H41N05</td>
<td>459.625</td>
<td>-</td>
<td>Mp-276-278</td>
</tr>
<tr>
<td>4.</td>
<td>Uttroside B</td>
<td>C56H94O28</td>
<td>1215.342</td>
<td>Crystal</td>
<td>Mp-210-215</td>
</tr>
<tr>
<td>5.</td>
<td>Uttroside A</td>
<td>C57H96O28</td>
<td>1229.369</td>
<td>Crystal</td>
<td>Mp-220-225</td>
</tr>
<tr>
<td>6.</td>
<td>2”-O-α-L-Rhamnopyranosyl</td>
<td>C27H30O16</td>
<td>610.524</td>
<td>Yellow needles</td>
<td>Mp-205-207</td>
</tr>
<tr>
<td>7.</td>
<td>2”-O-α-L-Rhamnopyranosyl, 6”-O-β-D-glucopyranosyl</td>
<td>C33H40O20</td>
<td>772.666</td>
<td>Brown powder</td>
<td>-</td>
</tr>
<tr>
<td>8.</td>
<td>β - Solanigrine</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>9.</td>
<td>α - Solanigrine</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>10.</td>
<td>12-β-Hydroxy, 23-acetoxy</td>
<td>C29H45O5</td>
<td>487.678</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>11.</td>
<td>Alkaloid SN-e</td>
<td>C45H73N017</td>
<td>900.068</td>
<td>Amorphous Powder</td>
<td>-</td>
</tr>
<tr>
<td>12.</td>
<td>Uttronin A</td>
<td>C50H82O22</td>
<td>1035.185</td>
<td>Crystal</td>
<td>Mp-241-245</td>
</tr>
</tbody>
</table>

TRADE AND COMMERCE-

Generally, in the market wet herb is not available, but it can be seen in vegetable market. The dried fruits are available all the time in market. Retail market price of the whole plant is Rs. 42/- per Kg and Seeds for Rs. 200/- per Kg. (2000) 105
PROPAGATION AND CULTIVATION

It is a prolific seed bearer having a high germination rate. It is thus easy to propagate this plant by seed. The seeds may be shown in March-April and transplantation of seedling raised in nursery may be done in June-July. Though the plant tolerates variety of soil, it prefers well-drained light soil. Calli of *S. nigrum* were initiated from leaf, stem and sepal explant on B5 media, containing varying concentration of 2,4-D and kinseyin. The leaf explants were found most suitable for callus inhibition and callus growth in comparison to stem and stem explants. The explants were well suited to an early callus initiation and showed better potential for regeneration as it produced plantlets from leaf discs on B5 medium containing NAA (0.01-0.5 mg/l. The leaf calli were further cultured on B5 medium containing 2,4-D for three passages, further the plantlets were regenerated from 3rd passage calli.

MS basal medium containing BA and NAA (0.5 mg/ml each) was found to be the best for the production of *Solanum nigrum*. A series of in vitro and in vivo plants were usefully produced and chemical analysis revealed contents of glycoalkaloids higher than those reported for intact field plants.

SULPHONYL UREAS

History:

In contrast to the systematic studies that led to the isolation of insulin, the sulfonylureas were discovered accidentally. In 1942, Janbon and colleagues noted that some sulfonamides caused hypoglycemia in experimental animals. These observations were soon extended, and 1-butyI-3-sulfonylurea (carbutamide) became the first clinically useful sulfonylurea for the treatment of diabetes. This compound was later withdrawn because of adverse effects on the bone marrow, but it led to the development of the entire class of sulfonylureas.

Mechanism of Action -

Sulfonylureas cause hypoglycemia by stimulating insulin release from pancreatic cells. Their effects in the treatment of diabetes, however, are more complex. The acute administration of sulfonylureas to NIDDM patients increases insulin release from the pancreas. Sulfonylureas also may further increase insulin levels by reducing hepatic
clearance of the hormone. In the initial months of sulfonylurea treatment, fasting plasma insulin levels and insulin responses to oral glucose challenges are increased. With chronic administration, circulating insulin levels decline to those that existed before treatment, but, despite this reduction in insulin levels, reduced plasma glucose levels are maintained. The explanation for this is not clear, but it may relate to reduced plasma glucose allowing circulating insulin to have more pronounced effects on its target tissues, and to the fact that chronic hyperglycemia per se impairs insulin secretion.

It should be noted that there is no measurable acute stimulatory effect of sulfonylureas on insulin secretion during chronic treatment. This is thought to be due to down regulation of cell surface receptors for sulfonylureas on the pancreatic β-cell. If chronic sulfonylurea therapy is discontinued, pancreatic β-cell responsiveness to acute administration of the drug is restored. This raises the question of whether or not NIDDM patients who are responding poorly to maximal doses of a sulfonylurea would benefit from a short period of withdrawal from the drug. Sulfonylureas also stimulate release of somatostatin, and they may suppress the secretion of glucagon slightly.

The effects of the sulfonylureas are initiated by binding to and blocking an ATP-sensitive K⁺ channel, which recently has been cloned. The drugs thus resemble physiological secretagogues (e.g., glucose, leucine), which also lower the conductance of this channel. Reduced K⁺ conductance causes membrane depolarization and influx of Ca²⁺ through voltage-sensitive Ca²⁺ channels.

There has been controversy about whether or not sulfonylureas have clinically significant extrapancreatic effects. The concentration of insulin receptors increases in the monocytes, adipocytes, and erythrocytes of NIDDM patients who receive oral hypoglycemic agents. Sulfonylureas enhance insulin action in cells in culture and stimulate the synthesis of glucose transporters. Sulfonylureas also have been shown to suppress hepatic gluconeogenesis; however, it is not clear if this is a direct effect of the drug or a reflection of increased sensitivity to insulin. In general, attempts to ascribe the long-term blood glucose-lowering effects of sulfonylureas to specific changes in insulin action on target tissues are confounded by the effects of a lowered prevailing blood glucose level. Although extra pancreatic effects of sulfonylureas can be demonstrated, they are of minor clinical significance in the treatment of NIDDM patients.
Absorption, Fate, and Excretion

The sulfonylureas have similar spectra of activities; thus, their pharmacokinetic properties are their most distinctive characteristics. Although there are differences in the rates of absorption of the different sulfonylureas, all are effectively absorbed from the gastrointestinal tract. However, food and hyperglycemia can reduce the absorption of sulfonylureas. (Hyperglycemia per se inhibits gastric and intestinal motility and thus can retard the absorption of many drugs.) In view of the time required to reach an optimal concentration in plasma, sulfonylureas with short half-lives may be more effective when given 30 minutes before eating. Sulfonylureas in plasma are largely (90% to 99%) bound to protein, especially albumin; plasma protein binding is least for chlorpropamide and greatest for glyburide. The volumes of distribution of most of the sulfonylureas are about 0.2 liter/kg.

The first-generation sulfonylureas vary considerably in their half-lives and extents of metabolism. The half-life of acetohexamide is short, but the drug is reduced to an active compound with a half-life that is similar to those of tolbutamide and tolazamide (4 to 7 hours). It may be necessary to take these drugs in divided daily doses. Chlorpropamide has a long half-life (24 to 48 hours). The second-generation agents are approximately 100 times more potent than are those in the first group. Although their half-lives are short (1.5 to 5 hours), their hypoglycemic effects are evident for 12 to 24 hours, and it is often possible to administer them once daily. The reason for the discrepancy between the half-life and duration of action of these drugs is not clear.

The liver metabolizes all of the sulfonylureas, and the metabolites are excreted in the urine. Metabolism of chlorpropamide is incomplete, and about 20% of the drug is excreted unchanged. Thus, sulfonylureas should be administered with caution to patients with either renal or hepatic insufficiency.

Adverse Reactions

Adverse effects of the sulfonylureas are infrequent, occurring in about 4% of patients taking first-generation drugs and perhaps slightly less often in patients receiving second-generation agents. Not unexpectedly, sulfonylureas may cause hypoglycemic reactions, including coma. This is a particular problem in elderly patients with impaired hepatic or renal function who are taking longer-acting sulfonylureas. Sulfonylureas can
be ranked in order of decreasing risk of causing hypoglycemia based on their half-lives. The longer the half-life, the more likely an agent will induce hypoglycemia. Severe hypoglycemia in the elderly can present as an acute neurologic emergency that may mimic a cerebrovascular accident. Thus, it is important to check the plasma glucose of any elderly patient presenting with acute neurologic symptoms. Owing to the long half-life of some sulfonylureas, it may be necessary to treat an elderly hypoglycemic patient for 24 to 48 hours with an intravenous glucose infusion.

A number of other drugs may potentiate the effects of the sulfonylureas, particularly the first-generation agents, by inhibiting their metabolism or excretion. Some drugs also displace the sulfonylureas from binding proteins, thereby increasing the free concentration transiently. These include other sulfonamides, clofibrate, dicumarol, salicylates, and phenylbutazone. Other drugs, including ethanol, may enhance the action of sulfonylureas by causing hypoglycemia.

Other side effects of sulfonylureas include nausea and vomiting, cholestatic jaundice, agranulocytosis, aplastic and hemorrhagic anemias, generalized hypersensitivity reactions, and dermatological reactions. About 10% to 15% of patients who receive these drugs, particularly chlorpropamide, develop an alcohol-induced flush similar to that caused by disulfiram. Sulfonylureas, especially chlorpropamide, also may induce hyponatremia by potentiating the effects of antidiuretic hormone on the renal collecting duct. This undesirable side effect occurs in up to 5% of all patients; it is less frequent with glyburide and glipizide. This side effect has been used to therapeutic advantage in patients with mild forms of Diabetes Insipidus.

An unresolved question is whether treatment with sulfonylureas is associated with increased cardiovascular mortality; this possibility was suggested by a large multicenter trial (the University Group Diabetes Program or UGDP). The UGDP was designed to compare the effect of diet, oral agents (tolbutamide or phenformin), and fixed-dose insulin therapy on the development of vascular complications in NIDDM. During an 8-year period of observation, patients who received tolbutamide had a twofold higher rate of cardiovascular death than patients treated with placebo or insulin. A 10-year debate followed on the validity of this conclusion, because the observation was unexpected, the study had not been designed to test this question, and all of the excess mortality occurred
in only three centers. Although no comparable study has completely refuted this observation, most physicians continue to use oral hypoglycemic agents, since there are few therapeutic options other than insulin for the NIDDM patient who has failed dietary therapy.

**Therapeutic Uses**

Sulfonylureas are used to control hyperglycemia in NIDDM patients who cannot achieve appropriate control with changes in diet alone. In all patients, however, continued dietary restrictions are essential to maximize the efficacy of the sulfonylureas. Some physicians still consider treatment with insulin to be the preferred approach in such patients. Patients with NIDDM whose disease is controlled with relatively low doses of insulin (less than 40 U per day) are more likely to respond to sulfonylureas, as are those who are obese and/or over 40 years of age. Contraindications to the use of these drugs include IDDM, pregnancy, lactation, and significant hepatic or renal insufficiency.

Between 50% and 80% of properly selected patients will respond initially to an oral hypoglycemic agent. All of the drugs appear to be equally efficacious. Concentrations of glucose often are lowered sufficiently to relieve symptoms of hyperglycemia, but they may not reach normal levels. To the extent that complications of diabetes may be related to hyperglycemia, the goal of treatment should be normalization of both fasting and postprandial glucose concentrations. However, since there are few therapeutic options, physicians frequently will continue treatment with a sulfonylurea in patients who have persistent, mild-to-moderate hyperglycemia. About 5% to 10% of patients per year who respond initially to a sulfonylurea become secondary failures, as defined by unacceptable levels of hyperglycemia. This may occur as a result of a change in drug metabolism, progression of β-cell failure, change in dietary compliance, or misdiagnosis of a patient with slow-onset IDDM. Changing to another oral agent will occasionally produce a satisfactory response, but most of these patients will eventually require insulin.

The usual initial daily dose of tolbutamide is 500 mg, while 3000 mg is the maximally effective total dose; corresponding doses for acetohexamide are 250 and 1500 mg. Tolazamide and chlorpropamide are usually administered in a daily dose of 100 to 250 mg, while 750 to 1000 mg is maximal. Tolbutamide, acetohexamide, and tolazamide
are often taken twice daily, 30 minutes before breakfast and dinner. The initial daily dose of glyburide is 2.5 to 5 mg, while daily doses of more than 20 mg are not recommended. Therapy with glipizide is usually initiated with 5 mg given once daily. The maximal recommended daily dose is 40 mg; daily doses of more than 15 mg should be divided. The starting dose of gliclazide is 40 to 80 mg per day, and the maximal daily dose is 320 mg. Treatment with the sulfonylureas must be guided by the individual patient's response, which must be monitored frequently.

References-


24. Charaka Samhita, Vimanasthana 8/143
25. Charaka Samhita, Sutrasthan 27/90
26. Charaka Samhita, Chikitsasthana 14/124
27. Charaka Samhita, Chikitsasthana 18/81
28. Charaka Samhita, Chikitsasthana 27/27
29. Charaka Samhita, Chikitsasthana 29/53
30. Charaka Samhita, Sutrasthana 3/17
31. Charaka Samhita, Chikitsasthana 7/96
32. Charaka Samhita, Chikitsasthana 12/71
33. Charaka Samhita, Chikitsasthana 21/90
34. Charaka Samhita, Chikitsasthana 26/269
35. Charaka Samhita, Sutrasthana 26/83
36. Charaka Samhita, Nidanasthana 5/6
37. Charaka Samhita, Chikitsasthana 16/85
38. Sushruta Samhita, Sutrasthana 46/262
39. Sushruta Samhita, Sutrasthana 38/18
40. Sushruta Samhita, Sutrasthana 20/13-14
41. Aattang Hrudaya Sutrasthana 6/14, 7/35, 15/30. Chi 19/63, U 22/2. 39/141
42. Gadamigraha, Rasayanatantrya Oushadhikalpadhikara 2.
43. Astang Nighantu / 32
44. Dhanvantari Nighantu, Karaveeradi Chaturtha Varga / 19
45. Amarkosha, 2nd Kand, Vanoushadhi Varga, 4/151
46. Shodhal Nighantu, Karaveeradi Varga
47. Madanpal Nighantu, Abhayadi Varga / 51
50. Raj Nighantu, Shatavhadi Chaturtha Varga / 37
51. Shaligram Nighantu, Guduchyadi Varga Part 7-8, p 332.
52. Abhinava Nighantu, p 132.
53. Priyanighantu, Shatapushpadi Varga / 147.
55. Rasaratnasamuchchaya-29/143
56. Rasaratnasamuchchaya -11/58
57. Rasaratnasamuchchaya -12/68
58. Rasaratnasamuchchaya -14/3
59. Rasaratnasamuchchaya-16/90
60. Rasaratnasamuchchaya-18/150
61. Rasaratnasamuchchaya -20/52
62. Rasaratnasamuchchaya -21/32
63. Rasaratnasamuchchaya -26/8
64. Rasaratnasamuchchaya -29/115
65. Rasaratnasamuchchaya -30/66
66. Rasatarangini 5/91
68. Rasatarangini 7/99.
69. Rasatarangini 10/43
70. Rasatarangini 10/56
71. Rasatarangini 13/95

88. *Charaka Samhita*, Sutrasthana 27/89
89. *Susruta Samhita*, Sutrasthana 46/266
90. *Astang Samgraha*, Sutrasthana 7/133.
91. *Astang Hridaya*, Sutrasthana 6/74
92. *Dhanvantari Nighantu*, Karaveeradi Chaturtha Varga /19
93. *Shodhal Nighantu*, Karaveeradi Varga
95. *Madanpala Nighantu*, Abhayadi Varga /51
96. *Raj Nighantu*, Shatavhari Chaturtha Varga /37
97. Madhava Dravyaguna, Shaka Varga 22/7
99. *Nighantu Adarsha*, Uttarardhda, p. 134
100. *Nighantu Ratnakara*, Guduchyadi Varga
103. Priya Nighantu, Shatapushpadi Varga / 147
104. Shaligram Nighantu, Guduchyadi Varga Part 7-8, p 332.
106. Anon, Wealth of India, p. 391. Publication & Informatics directorate CSIR, New Delhi, 1976
107. Charaka Samhita, Sutrasathana 26/83
108. Charaka Samhita, Nidanasthana 5/6
109. Charaka Samhita, Chikitsasthana 16/85
110. Susruta Samhita, Sutrasathana 20/13-14
111. Gadanigraha Guitikadhihikara /245
112. Nighantu Adarsha, Uttarardhda, p. 134
113. Bhavaprakasha Nighantu, Poorva Khand 6/ 98-104
115. Charaka Samhita, Sutrasathana 3/17
116. Charaka Samhita, Sutrasathana 7/96
117. Charaka Samhita, Chikitsasthana 26/269
118. Bhavaprakasha Chikitsasthana Madhyakhand Jwararogadhihikara / 327
120. Anon, Wealth of India, p. 391, Publication & Informatics directorate CSIR, New Delhi, 1976