PHARMACOLOGICAL APPRAISAL OF CUMINUM CYMINUM L. IN DYSEMENORRHOEA: AN AYURVEDIC APPROACH IN CONSIDERATION OF CURRENT EVIDENCES

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ABSTRACT
The demand of personalized medication has grown to leaps and bounds since last few years. Ayurveda, the oldest system of medicine, emphasized on such personalized medication by analyzing the personal health status of individual through different assessment criteria. Cuminum cyminum L. called as Jeeraka in Sanskrit and Jeera in Hindi, is one of the herb which was used since many centuries for various ailments. Traditionally the herb is well-known for its action in various alimentary diseases like, indigestion, diarrhea, gynecological diseases, etc. This herb is also screened for various pharmacological activities like antibacterial, anticancer, antulcer and others. The condition of painful menstruation is affecting more than half of young adolescent girl population. The current article is an effort to establish the mode of action of Cuminum cyminum L. in terms of Ayurveda pathogenesis as well as contemporary science. Various pathogenic pathways of Dysmenorrhoea according to Ayurveda are discussed with conclusion of using Jeeraka in dysmenorrhoea under which particular pathogenesis. Such comparison will help to establish personalized medicine for other diseases and this may be a novel approach towards same.

KEYWORDS: Cuminum cyminum L., Jeeraka, Individualized/Personalized medicine, Dysmenorrhoea, Menstrual Pain.

INTRODUCTION
The present status of chronic diseases in relation with availability of their treatment-approaches is observed to be very limited [1]. Despite of having many technological developments in current science, the exact cure of these diseases is not achieved. Moreover various patterns of symptomatic relief of diseases persist in the existing scenario. As a reflection, gradually, the world is taking interest in the culture of Individualized / Personalized Medicine and trying to get relief from many diseases [2,3]. The Ayurveda claimed Individualized / Personalized Medicine is a science, based on the concepts for analyzing the various parameters mentioned in literature. Eventually, the classical Ayurveda lies in implementing these selective methods and providing proper remedy in proper form to the needy. It will be always encouraged and appreciated that the selection of herb must have some evidence based background to convince the new generation. However, it doesn’t always mean that the selected herb must have or must not have the proved back-up for claimed actions. So far the contemporary way of Herbal Research is concerned, it is found to be still in infancy to validate Ayurvedic claims with respect to the concepts of Ayurveda. In Ayurveda, the knowledge regarding personified-study is mentioned under the concept ‘Amshamsha Vikalpana’ which covers a broad range of human as well as drug study. The human differential factors are achieved through Vyadhi Ghataka (factors responsible for pathogenesis), where as drug selection is achieved by Rasapanchaka (Ayurvedic conceptual composition of herb). Ayurveda the science of life have greatness in studying pathogenesis and selection of remedy accordingly. At primary level, with an example of Dysmenorrhoea, this theme is attempted by evaluating various pathological conditions of Ayurveda and contemporary sciences supported by the pharmacological claims of Cuminum cyminum L.

Glimpse of Dysmenorrhoea
Prevalence: Dysmenorrhoea is one of pathological condition which is generally ignored by patients and practically unresolved completely by physicians (except some pathology). It is observed through various published paper that the dysmenorrhoeal condition is present throughout the world [4]. According to a survey, an average of 68% girls has dysmenorrhoea and alarming one in eight girls reported absenteeism at college/school because of menstrual symptoms [5].

Ayurvedic View
The condition of dysmenorrhoea is explained in Ayurvedic literature in terms of ‘Kastartava / Kukshi Shoola, Vatala Yoni, Udavartini Yonyiapad’ (Ayurvedic names of disease under Striroga-Gynecology) [6]. The causative factors, pathogenesis, symptoms and treatment are also described in Ayurveda and based on that, the increased ‘Yata’ type of humors in the body is responsible for disease creation [7]. The various Ayurvedic causative factors which manifest into dysmenorrhoea are inappropriate food habits, inappropriate lifestyle,
Infectious menstruation, vitiated reproductive physiology, abnormal ovarian function, inappropriate sitting-sleeping habits, excessive use of liquid foods and many non-etiologic factors. All these factors create imbalance in humors (Vata-Pitta-Kapha) of a normal individual through specific mode of vitiations. This vitiation may occur by individual-increase of body-humors (Vata-Pitta-Kapha) or their combinations. The modes of vitiations are called as Samprapti or Dosh-Dushya Sammurchhana (pathogenesis). This pathogenesis of Kashtartava can be summarized under six major patterns. The aim of management should be by equilibrating vitiated Doshas, especially Vata (as it is main causative factor of all Yonivyapadas) or managing Avrita Apana Vayu (pathology of one of the type of Vata humor) through Agnideepaka (improving appetite), Grahi (controlling of excessive outflow), Vata Anulomana (normalizing any type of abnormal flow) and Pakvashaya Shuddhikara (purification of large intestine) methods.

Contemporary Medicine

The various causes of Dysmenorrhoea described under contemporary system of medicine are like environmental factors causing nervous tension, general ill health, faulty outlook, hormonal imbalance, psychogenic cause, imbalance of autonomic nervous system, intruterine contraceptive device, stenosis at internal Os, unequal development of Mullerian ducts, inappropriate low of polarity, retroverted uterus, uterine hypoplasia, vasopressin and prostaglandins.

Ayurvedic Individualized / Personalized Medicine

Ayurveda advocates that selection of any medicine should be purely based on the Individualized / Personalized features of sufferings. According to Charaka Samhita a best physician should know the science of administration of drugs with due reference to climate and season, and who applies it only after examining each and every patient individually. Moreover while commenting on the role of diet, Charaka recommends planning of opposite properties of vitiated Doshas in the form of diet to maintain the health. Habitual intake of balanced diet with all Rasas (tastes) in proportionate quantity is recommended for equilibrium of doshas. The Ayurveda system does not stress on the naming of the disease but a proper diagnosis related with the vitiation is more important than the labeling of the disease. It explains that the diseases are innumerable being divided on the basis of trouble, color, etiology, site, symptoms and name. However in other cases general principle may be followed.

Ultimately, applying knowledge and common sense one should plan the management. Moreover, the treatment should be continued till the patient regains health. While describing the state of normalcy Ayurveda screened many points to identify healthy individual. Some of these parameters like person having good built, has balanced proportion of muscles, compactness of the body, possess very strong sensory and motor systems, etc. Also healthy individual can withstand hunger, thirst, the heat of the sun, cold and physical exercise. They can digest and assimilate the food properly. In total all these factors make the concept of Individualized / Personalized features of an individual and help in assessment of personalized treatment plan. In the present paper we adopted some methods to achieve the target through literature review.

Methodology

Based on the above information the conceptual analysis of Dysmenorrhoea (disease) and Jeeraka (drug as a remedy) was studied with detailed micro-classification. The pathogenesis of Kashtartava (Dysmenorrhoea) condition was classified based on the basic concepts of Ayurveda so that exact pathology can be understood (Table No. 1). The disease pathology was broadly classified into six major categories (Images). The Samprapti Ghataka (factors responsible for disease formation) was further correlated with pinpointed (broad category of Individualized / Personalized) pathological conditions of Kashtartava with special reference to type of pathology (Table No. 2).

On the other hand, the literature analysis on herb Cuminum cyminum L. (Jeeraka) was conducted. The properties and pharmacological indications were noted down (Table No. 3). A comparative estimation was calculated among the desired properties of the drug needed in various pathological conditions of Kashtartava (Dysmenorrhoea) and the properties present in Jeeraka. An interpretations was also made for logical application of the drug in specific conditions (Table No. 4).

To support the Ayurvedic theme of Jeeraka selection in Kashtartava (Dysmenorrhoea), a review regarding its pharmacological screening was conducted. No direct references were found regarding its activity on signs / symptoms of Dysmenorrhoea. But a conceptual indirect pharmacological activity references were collected which may claim the action in the diseased condition (Table No. 5). Some review of essential / non essential activities were also studied to know the efficacy of Jeeraka in terms of modern experimental study. Some of the activity was absolutely not found, neither their relations can be made with the Dysmenorrhoea condition.

**Table 1: Samprapti Ghataka (factors responsible for Kashtartava (Dysmenorrhoea) pathogenesis)**

<table>
<thead>
<tr>
<th>No</th>
<th>Conceptual head of Factors</th>
<th>Type of vitiation under the head</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Dosa (Body humors)</td>
<td>Vata Pradhana Tridoshha</td>
</tr>
<tr>
<td>2.</td>
<td>Dushya (tissues / cells involved)</td>
<td>Rasa, Rakta, Artava</td>
</tr>
<tr>
<td>3.</td>
<td>Agni (digestive capacity)</td>
<td>Jatharagni, Dhatvagni Mandya</td>
</tr>
<tr>
<td>4.</td>
<td>Srotasa (systems involved)</td>
<td>Rasa, Rakta and Artavavaha Srotasa</td>
</tr>
<tr>
<td>5.</td>
<td>Srotodushiti (mode of system involvement)</td>
<td>Sanga and Vimargagama</td>
</tr>
<tr>
<td>6.</td>
<td>Udbhavasthana (root cause of origin of pathology)</td>
<td>Amapakvashaya</td>
</tr>
<tr>
<td>7.</td>
<td>Sthana Samshraya (place where the disease expressed)</td>
<td>Garbhashaya</td>
</tr>
<tr>
<td>8.</td>
<td>Vyakti Sthana (labeling of the disease)</td>
<td>Triyavarta Yoni</td>
</tr>
</tbody>
</table>

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Table 2: Micro-classification of Kashatartava Pathology in Ayurveda

<table>
<thead>
<tr>
<th>Type of pathogenesis</th>
<th>Dosa</th>
<th>Dushya</th>
<th>Agni</th>
<th>Srotos-Gamitva</th>
<th>Eradication of Srotodushti</th>
<th>Acting place of Uddhavasthana</th>
<th>Sthana Samshraya (Broad area)</th>
<th>Vyaktasthana (Specific area)</th>
<th>Lakshana (Symptom)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ayurveda Pathogenesis 1</td>
<td>Vata</td>
<td>Shamaka</td>
<td>Agni</td>
<td>Rasa, Rakta</td>
<td>Dhatvagni</td>
<td>Vayama</td>
<td>Rasa-Rakta Dhautu</td>
<td>Sampurna Shareera</td>
<td>Garbhashaya</td>
</tr>
<tr>
<td>Ayurveda Pathogenesis 2</td>
<td>Vata</td>
<td>Shamaka</td>
<td>Agni</td>
<td>Rasa, Rakta</td>
<td>Dhatvagni</td>
<td>Vayama</td>
<td>Rasa-Rakta Dhautu</td>
<td>Sampurna Shareera</td>
<td>Garbhashaya</td>
</tr>
<tr>
<td>Ayurveda Pathogenesis 3</td>
<td>Pitta-Vata</td>
<td>Shamaka</td>
<td>Agni</td>
<td>Rasa, Rakta</td>
<td>Artava</td>
<td>Vayama</td>
<td>Rasa-Rakta Dhautu</td>
<td>Sampurna Shareera</td>
<td>Garbhashaya</td>
</tr>
<tr>
<td>Ayurveda Pathogenesis 4</td>
<td>Kapha</td>
<td>Vata</td>
<td>Agni</td>
<td>Rasa, Rakta</td>
<td>Dhatvagni</td>
<td>Vayama</td>
<td>Rasa-Rakta Dhautu</td>
<td>Sampurna Shareera</td>
<td>Garbhashaya</td>
</tr>
<tr>
<td>Ayurveda Pathogenesis 5</td>
<td>Sansarga</td>
<td>or Sannipata</td>
<td>Agni</td>
<td>Rasa, Rakta</td>
<td>Dhatvagni</td>
<td>Vayama</td>
<td>Rasa-Rakta Dhautu</td>
<td>Sampurna Shareera</td>
<td>Garbhashaya</td>
</tr>
<tr>
<td>Ayurveda Pathogenesis 6</td>
<td>Vata</td>
<td>Shamaka</td>
<td>Agni</td>
<td>Rasa, Rakta</td>
<td>Dhatvagni</td>
<td>Vayama</td>
<td>Rasa-Rakta Dhautu</td>
<td>Sampurna Shareera</td>
<td>Garbhashaya</td>
</tr>
</tbody>
</table>

Table 3: Jeeraka: The Ayurvedic records

<table>
<thead>
<tr>
<th>No</th>
<th>Properties &amp; Actions</th>
<th>Criteria</th>
<th>Quotes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pharmacological Properties</td>
<td>Rasa</td>
<td>Katu21,22,23,24,25 Tikta21</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gunas</td>
<td>Ruksha21,22,23,24 Lagha21,23,24</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Veerya</td>
<td>Ushna21,22,23,24,25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vipaka</td>
<td>Ushna Paka21</td>
</tr>
<tr>
<td>2</td>
<td>Pharmacological Actions</td>
<td>On Humors (Doshaghnata)</td>
<td>Pittala21,22,23,24 Vata-Kapahara21 Vatahara22,23,24,25 Kaphahara22,23,24</td>
</tr>
</tbody>
</table>

Table 4: The Samprapti Ghataka (factors responsible for Dysmenorrhoea pathogenesis)

<table>
<thead>
<tr>
<th>No</th>
<th>Desired action on Dysmenorrhoea</th>
<th>Actions of Jeeraka</th>
<th>Classical interpretation of Jeeraka actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vata Pradhana Tridosha</td>
<td>Vata-Kapahara</td>
<td>The Drug will specifically applicable only in Vata-Kapha dominant Kashtartava (Dysmenorrhoea) condition.</td>
</tr>
<tr>
<td>2</td>
<td>Rasa, Rakta, Artava</td>
<td>Pachana</td>
<td>The drug will not nourish the Rasa-Rakta Dhatu but will improve its functional capacity. It will be utilized for limited period till the condition gets normalize.</td>
</tr>
<tr>
<td>3</td>
<td>Jatharagni, Dhatvagni Mandy</td>
<td>Deepana21,22,23,24,25, Pachana21,23,24,25</td>
<td>Through the Main Agni (Jatharagni), Jeeraka will start showing its action. Eradication of root cause in the form of malfunction of Mahasrotasa it shows its results. Normalizing metabolism may be the main effect.</td>
</tr>
<tr>
<td>4</td>
<td>Rasa, Rakta and Artavavahaa Srotasaa</td>
<td>Garbhashaya Vishodhana21,23,24</td>
<td>The drug shows action specifically on Uterus by removing the metabolic toxicity. It helps in improving regular menstrual blood flow, improvement in menstruation complications. Improving the Dhatvagni of Rasa-Rakta Dhatu is the main area of the drug.</td>
</tr>
</tbody>
</table>
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6. Amapakvashaya
   - Katu\textsuperscript{21,22,23,24,25}
   - Tikta\textsuperscript{21} Ushna\textsuperscript{21,22,23,24,25}
   - Pachana\textsuperscript{21,23}

These references show the main action is on Mahasrotasa (Annavaaha). Which facilitate in eradication of Ama (endotoxins) and formation of new, sustainable, puriofied Dhatus which later helps in improving the disease condition.

7. Garbhashaya
   - Garbhashaya Vishodhana\textsuperscript{21,23,24}

By purifying and cleansing the uterus (Garbhashaya Vishodhana) it helps in creation of ideal platform for normal menstruation, development of good progeny, etc.

Table 5: Pharmacological screening of jeeraka

<table>
<thead>
<tr>
<th>No.</th>
<th>Pathogenesis factor</th>
<th>Direct or indirect references of Pharmacological actions useful in pathogenesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Hormonal Imbalance</td>
<td>Galactogogues\textsuperscript{26}  &lt;br&gt; Sperm Function\textsuperscript{27}  &lt;br&gt; Antitesticular\textsuperscript{28}  &lt;br&gt; Anti-estrogenic\textsuperscript{29}  &lt;br&gt; Anti-osteoporotic\textsuperscript{30}</td>
</tr>
<tr>
<td>2.</td>
<td>Ischaemic Theory</td>
<td>Erythrocyte Hemolysis\textsuperscript{31}  &lt;br&gt; Blood Platelet Aggregation\textsuperscript{32}  &lt;br&gt; Hypolipidemic\textsuperscript{33,34}</td>
</tr>
<tr>
<td>3.</td>
<td>Psychogenic Causes</td>
<td>Antistress\textsuperscript{35}  &lt;br&gt; Alzhiemer\textsuperscript{36}  &lt;br&gt; Central Nervous system\textsuperscript{37,38,39}</td>
</tr>
<tr>
<td>4.</td>
<td>Prostaglandins (PGs)</td>
<td>Analgesic\textsuperscript{40,41}  &lt;br&gt; Antinflammatory\textsuperscript{42}</td>
</tr>
<tr>
<td>5.</td>
<td>Systemic Disease and General Ill Health</td>
<td>Antibacterial Activity\textsuperscript{43,44}  &lt;br&gt; Antimicrobial\textsuperscript{45}  &lt;br&gt; Antifungal activity\textsuperscript{46}  &lt;br&gt; Antioxidant properties\textsuperscript{47}  &lt;br&gt; Immunomodulatory\textsuperscript{48}</td>
</tr>
<tr>
<td>6.</td>
<td>Other indirect activities</td>
<td>Hepatoprotective\textsuperscript{49,50,51}  &lt;br&gt; Antidiabetic\textsuperscript{52}  &lt;br&gt; Antiepileptic\textsuperscript{53}  &lt;br&gt; Gastrointestinal Disorders\textsuperscript{54,55}  &lt;br&gt; Antiulcer\textsuperscript{56}  &lt;br&gt; Antidermatophytic\textsuperscript{57}  &lt;br&gt; Anticancer\textsuperscript{58}</td>
</tr>
<tr>
<td>7.</td>
<td>Myometrial Activity Theory</td>
<td>No direct reference found</td>
</tr>
<tr>
<td>8.</td>
<td>Vasopressin</td>
<td>No direct reference found</td>
</tr>
<tr>
<td>9.</td>
<td>Poor Posture</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>10.</td>
<td>Abnormal Anatomical And Functional Aspects of Uterus</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>11.</td>
<td>Muscular In-coordination</td>
<td>Not Available</td>
</tr>
</tbody>
</table>

Ayurveda Pathogenesis - 1

**VATA VRIDDHI FACTORS**
- Vata Prakopa
- Dhatushaya
- Rasa Kshaya
- Rakta Kshaya
- Upadhatu-Artha Kshaya
- Vata Prakopa
- Stodanam Sa Vedanam Artava Pravritti (Dysrhythmia of uterine muscles)

**PITTA VRIDDHI FACTORS**
- Vata Prakopa
- Rasavaha, Rakshavaha and Arnavaha Srotodushit
- Vibration of Vyana and Apana Vayu
- Disturbance in Aksanchara and Prasarnaravirya of Garbhshaya
- Stodanam Sa Vedanam Artava Pravritti (Dysrhythmia of uterine muscles)

**KASHTARTAVA**
DISCUSSION & CONCLUSION

There are many herbs that are directly or indirectly indicated in the menstrual condition, especially Kashtartava (Dysmenorrhea). Jeeraka i.e. Cuminum cyminum L. is one of the popular herbs used since many centuries for various ailments as mentioned in Ayurveda literature. Based on the properties of the herbs, it shows its action through the pacifying many abnormal conditions of Gastro-intestinal tract. This GIT is considered as Mahasrotasa (Major channel) in Ayurveda and its dysfunction leads to many diseases. The various indications of Jeeraka like Ajeerna, Deepana, Pachana, Gulma, Garhani, Atisaara, Adhmana, Atopa, etc directly establish it as a drug of choice in GIT associated menstrual disease. By this way it not only pacifies the symptoms of disease but also rectify the root cause of disease. Apart from this it has direct action as Garbhshahaya Vishodhana which leads to clean the female reproductive system. Having targeted action on affected part as well as capacity to eradicate the disease from its root makes Jeeraka as one of the best choice of drug. While planning Jeeraka, one should observe its utility for a specific period. Being Ushna, Ruksha, Laghu, Katu, Tikta, it may harm and create Dhatukshaya by various manner. Hence though it is a good herb for Kashtartava, it should be administered only till the relief and should not be used excessively. The pharmacological screening for Sperm Function and anti-testicular activity is an additional proof for its side-effects in long term use. By studying the Ayurvedic pathology Jeeraka can be the best drug of choice in Pathology 2, better in pathology 4, good drug of choice in pathology 5 & 3. It should not be recommended in pathology 1 where Dhatukshaya is a responsible cause for disease. It also may not show its effects in pathology 6 where psychosomatic involvements are observed. The modern pharmacological screening can be correlated but can't be claimed to validate the Ayurvedic activities. Ayurvedic action of Jeeraka on menstrual disorder through GIT is a best example to discard the theory of correlation among two systems. The entire pathology of Dysmenorrhea is least concerned with GIT activity (exact opposite to Ayurveda). The screening strongly correlate the analgesic, anti-inflammatory, anti-microbial and Galactogogues activity. Overall both the sciences are helpful to know the nature of the disease and drug which help the researchers to think and plan a treatment for the betterment of society.

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