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ORIGINAL RESEARCH ARTICLE

A Comparative Study of *Berberis aristata* D.C. and *Berberis asiatica* Roxb.ex. D.C. (Daruharidra) W.S.R to Madhumehahara Karma

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ABSTRACT

Daruharidra has been mentioned in Prameha from shamita period to Nighantu Period. *Berberis aristata* D.C. is an official botanical source of Daruharidra, but some time *Berberis asiatica* Roxb.ex.D.C. is also used assuming same therapeutic potential. So here the stem of both species were studied Pharmacognostically, pharmaceutically, pharmacologically and clinically. The morphology of both plant vary in context of Leaves and Inflorescences. Microscopically also these two stem can be differentiated by difference in the architecture of Cork, cortex, medullary rays and presence of Rytidoma, prismatic crystal of calcium oxalate. Analytical study showed that the aqueous extract and berberine quantity is higher in the stem of *B.asiatica*. In pharmacological study the solidified aqueous extract of both species was compared, both have anti-hyperglycemic action but *B.aristata* has higher magnitude, however both drug didn't showed hypoglycemic in normal rats and Anti-diabetic action in alloxan induced diabetic rats. In clinical study 14 patients completed their treatment in each groups and Stem solidify aqueous extract (Ghana tablet) was given in the dose of 6gm/day for 6 weeks with Lukewarm water as anupana. Significant relief was seen in chief complaints and reduction in postprandial sugar levels in both the groups was observed, however reduction in fasting blood sugar and change in biochemical parameters were insignificant.

Key words: Daruharidra, *Berberis aristata* D.C., *Berberis asiatica* Roxb.ex.D.C, Prameha, Diabetes mellitus.

INTRODUCTION

The credibility of Ayurvedic system of medicine depends on the availability of authentic raw material in sufficient quantity, but in present scenario the market is full of substitute, Adulterant and spurious drugs. The reason may be the common vernacular name of different plants in various part of country. While classifying the drug botanically it is found that there were more than one species, belonging to same family, claiming the same classical name of the Ayurvedic drug and they are used without having any record of therapeutic potential. Keeping above view in mind, in this dissertation work the Daruharidra has been selected. The exact botanical source of Daruharidra by various Ayurvedic scholars is root of *Berberis aristata* D.C, but more than 13 species of berberis are available throughout Himalayan region ranging from 3,000-13,000ft Height. One of it is *Berberis asiatica*, which is considered as a substitute of *B.aristata* but no such scientific work has been done to prove it. Daruharidra has been mentioned in treatment of Prameha almost by all Acharyas. Hence in this study stem of *Berberis aristata* D.C. and *Berberis asiatica* Roxb.ex.D.C. will be studied pharmacognostically, and pharmaceutically. They will be evaluated for the Hypoglycemic, Anti-Hyperglycemic and Anti-diabetic action in animal models as well as for madhumehahara action in clinical study.

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AIM AND OBJECTIVE

1) To study pharmacognostically the stem of both species *Berberis aristata* D.C. and *Berberis asiatica* Roxb.ex.D.C. of Berberis.
(2) To carry out analytical study of the trial drugs.
(3) To evaluate the Hypoglycemic, Anti-Hyperglycemic, anti-diabetic action of both species in animal experiments.
(4) To assess clinically the Pramehaghan property of both species of Daruharidra.

MATERIALS AND METHODS

Pharmacognostical study

Mature stems of both species of *Berberis aristata* D.C. and *Berberis asiatica* Roxb.ex.D.C. were used as material for the present study and Conventional Pharmacognostic methods and procedures were used for the study of macro and microscopic characters of the both stem of plants.

Analytical Study

Pharmacognostically authenticated stem of both species *Berberis aristata* D.C and *Berberis asiatica* Roxb.ex D.C (Daruharidra) were used for the study. Kwatha was prepared from the dry stems, it was concentrated and then Ghanatablets were prepared. Those Ghanatablets were used in the present study. The samples were analyzed by employing various physico-chemical parameters and T.L.C. study.

Pharmacological study

The Kanda (Stem) Ghana-tablets of both species were obtained from the Gujarat Ayurved University's pharmacy from a single batch and were used throughout the experimental study. The dose selection was done on the basis of body surface area ratio using the table of Paget and Barnes. The test drugs and vehicle to control were administered according to the body weight of the animals by oral route with the help of gastric catheter. Charles Foster strain albino rats of either sex weighing between 190 – 290 g and Swiss albino mice of either sex weighing between 20 – 30 g were used for experiments. The rats and mice were divided into three groups i.e. Group-I *B.aristata*, Group-II *B.asiatica* Group-III Control, with six animals in each group to observe hypoglycemic action, Anti-hyperglycemic action and Anti-diabetic action in respective models.

Clinical Study

The patients were selected from the O.P.D. of Dravya Guna Department of I.P.G.T. & R.A and randomly divided in two groups, i.e. Group-I *B.aristata* Group-II *B.asiatica*, the drugs were in the form of stem ghana tablet, given in the dose of 6gm/day in three divided doses with lukewarm water as anupana for 6 weeks. Increase in Blood Sugar level either fasting or postprandial or both were the essential criteria for the selection. Exclusion criteria was fixed and routine, biochemical investigation were carried out to diagnose and assessment of the disease.

OBSERVATIONS

Pharmacognostical study

Macroscopically both plants can be easily differentiated, for microscopical study Transverse section was taken. The transverse section of both plants stem shows, multilayered cork, consisting of rectangular and squarish light yellowish to brownish colour thin walled cells arranged radially, inner most 3-5 layer of the cork cells are made up of highly thick walled and lignified cells .Cork cambium is not well evident. Cortex is narrow and made up of only 7-10 rows of tangentially elongated parenchyma cells. Few isolated highly thick walled narrow lumened stone cells also can be seen, scattered in the cortex. Phloem tissues are very wide in the lower region consisting of sieve tube, companion cells and parenchyma. They are narrow and major portion of it is made up of lignified sclerenchyma fibres. The Sclerenchyma fibres are arranged in tangential rows alternating with phloem elements. The tangentially arranged sclerenchyma fibres are 3-5 cells wide in the outer region and they become gradually narrow, with 1-2 rows in the lower region. Medullary rays are multiseriate consisting of 4-6 cell wide are passing through the phloem region and are obliquely or radially running towards the Xylem region. Medullary rays cells contain Prismatic crystal of calcium oxalate. Stone cells are also can be seen on either side of medullary rays especially in the Phloem region. Few rectangular thin walled cambium tissues also can be seen in between the phloem and xylem. Xylem occupies major portion of the stem and is made up of vessels, tracheids and wood fibres. The entire region is almost yellowish in colour and all the cells are highly lignified. The vessels in the secondary xylem are numerous, small-medium size distributed throughout the Xylem in group or in single. The group of vessels usually arranged radially. Isolated vessels are cylindrical in shape or projected at one or both ends, with spiral thickening. Xylem fibres numerous lignified, large and thick walled with narrow or wide lumen, Xylem rays are distinct straight and multiseriate consisting of radially arranged

rectangular cells. Some of the rays cells are highly thick walled and with pits. Prismatic crystals of calcium oxalate are also present occasionally in the medullary rays. In spite of this similarity *B.aristata* can be differentiated by presence of plenty prismatic crystal of calcium oxalate in cortex and inside the medullary rays cells, moreover it has wider Medullary rays as compare to the *B.asiatica*. However *B.asiatica* has Rhytidoma in the cork and starch grain in the xylem region.

Analytical study:

Analytical study of *Berberis aristata* D.C & *Berberis asiatica* Roxb. ex. D.C stem Ghana tablets was carried out under following parameters; Loss on drying at 110°C, Total ash value, Water soluble extract, Methanol soluble extract, Hardness of Gahan tablets, Tablet disintegration time, Average wt. of tablets. All values were almost similar in both Ghana tablets however the methanol extractive value was about 50% higher in *B.asiatica* as compared to *B.aristata*.

The water soluble extract of raw powder was more in *B.asiatica* (10.70%) as compare to *B.aristata* (5.95%).The Berberine amount is also more in *B.asiatica*(0.67%w/w) as compare to *B.aristata* (0.40%w/w). In TLC also similar spots were seen in both the species stem Ghana but the intensity was more in *B.aristata*.

Pharmacological study

• Test drugs on blood glucose level in the normal rats.

The blood sugar level was not affected to significant extent after test drug administration in normal rats at the dose level studied. In both the control and test drug administered group a moderate increase was observed at various time intervals at which blood sugar level was measured

• Test drugs on GTT in albino mice

In control group considerable hyperglycemia was observed at 45min, 90 min and 120 min in comparison to initial values. The percentage increase was 214.28 at 45 min, 156.22 at 90min and 100.96 at 120 minutes. In both the test drug administered groups though hyperglycemia was observed it was much less in comparison to control group especially at 90 and 120 min after glucose load.

In *B. aristata* administered group the increase was 50.55%, 80.16% and 69.65% less in comparison to control group at 45, 90 and 120 min post glucose load respectively. The difference in the increase between control group and *B. aristata* was found to be statistically significant with respect to the reading of 45 and 90 min.

In *B. asiatica* administered group the increase was 34.5%, 77.20% and 78.48 % less in comparison to control group at 45, 90 and 120 min post glucose load respectively. However the difference between this group and control was not significant at any of the time intervals at which readings were taken.

• Test drugs on blood sugar level in alloxan diabetic rats.

In control diabetic rats after eight days of vehicle treatment 59.22% increase in blood sugar level was observed. In *B. aristata* Ghana tablet administered group 59.29% increase in blood sugar level was observed, however in *B.asiatica* group 129.29% increase in blood sugar was observed.

• Biochemical parameters

Total thirteen biochemical parameters were assessed out of which 12 were measured in serum and one parameter in liver homogenate. Out of the 13 parameters studied significant changes due to drug administration was observed only in one that is Liver glycogen.

Clinical Study

Majority of the patients (47.22%) were reported in the age group of 41 – 50 years followed by 22.22% in the age group of 30-40 years. In present study maximum 33.33% of the patients were business man; followed by 30.56% were house wife. Majority of the patients i.e. 30.56% patients were reported to have a chronicity of 1 – 3 years and 3-5 years, followed by 22.22% having above 5 years, only 16.67% patients have chronicity of 1 year.

As B.M.I is concern only 36.11% patients were having normal weight, while 27.78% patients were obese, 25% were overweight and 13.89% patients were very obese. Shaka Sevana was seen in 72% of patients, followed by Guru Ahara (72.72%), Snigdha Ahara (61.11%), Ikshu Vikara (61.11%),however Sheeta Ahara, Madhura Ahara, Diwasapana, Avyayama were less frequent Nidana than formers. Among the Purva Rupa Mukh Talu Shosh, Dourbalyata, Kar-pad tal dah, and Visra Sharira Gandha was found in 27.78%, 25%, 19.44% and 19.44% respectively In chief complaints, Dourbalyata was found in maximum patients i.e. 69.44%, Prabhuta Mutrata was found in 58.33% patients, Kara-pada-tala-daha was found in 55.56%, Trishnadhikya was found in

44.44% of the patients, Kshudhadhikya was found in 30.56% of the patients. In present study 58.33% patients were having raised systolic blood pressure in the range of 130 – 150 mm/Hg, while 16.67% patients belonged to hypertensive group in the range of 150 – 170 mm/Hg and 61.11% patients were having raised diastolic blood pressure in the range of 91 –100 mm/Hg, while 16.67% patients belonged to hypertensive group in the range of 101 – 110 mm/Hg The mean fasting Blood Sugar level was 182.04 mg/dl and postprandial blood sugar was 265.28mg/dl. The mean S. cholesterol level was 205.61 mg/dl.

RESULTS

Pharmacological study

Berberis aristata and *Berberis asiatica* both reduces the blood sugar in sugar loaded rats but the reduction is significant in case of *B.aristata*. No hypoglycemic and antidiabetic action is observed in both drugs.

Clinical study

In each group 14 patients completed their treatment.

- Effect on chief complaints
  Berberis aristata Ghana tablet group provided statistically highly significant (P<0.001) relief in Prabhuta-mutrata by 83.47%, Kar-pad-tal-dah (86.40%) and Dourbalyata 62.50%), whereas significant relief was obtained in Kshudhadhikya and Trishnadhikya.
  B.asiatica tablet group provided statistically highly significant (P<0.001) relief in Prabhuta Mutrata by 59.02% relief and in Kar-pad tal-dah(62.71%).Statistically insignificant relief was in Kshudhadhikya (50%) and Dourbalyata (42.85%).
- Effect on Biochemical values
  Berberis aristata provided statistically insignificant reduction in Fasting blood sugar (0.40%) and S. Cholesterol level with percentage reduction of 4.42%. Significant reduction in postprandial Blood sugar level was seen with 11.87% relief (P<0.05). *Berberis asiatica* provided statistically insignificant reduction (P>0.05) in Fasting blood sugar by 4.92% relief and in the S. Cholesterol level with percentage reduction of 6.73%. Postprandial Blood sugar level was significantly decreased (P<0.05) with 16.39% relief.
- Effect On Hematological Values-
  In both *Berberis aristata* and *Berberis asiatica* Ghana tablet group provided statistically insignificant change in Hb%,T.L.C and E.S.R. However in *Berberis asiatica* group statistically significant (P<0.05) decrease was seen in E.S.R. (24.80%).

DISCUSSION

Analytical

The loss on drying of the sample was between 9-10%.This relates to the moisture content in the sample and the value is in higher side. The ash value of *B.aristata* was more (19.11%) as compared to that of *B.asiatica* indicating presence of more inorganic content in it. Both water and methanol soluble extractive of both the samples are quite high as expected since the tablets were prepared by using ghana i.e. water soluble extract, The methanol soluble extractive was about 50% higher in *B.asiatica* (47.55%) than *B.aristata* (33.41%). The data indicates that both water soluble extractive and berberine content was much higher in *Berberis asiatica i.e.* 10.70% and 0.67% respectively, as compare to 5.95% and 0.40% in *B.aristata* respectively. As could be seen from the chromatogram that the development pattern is same in both (*B.aristata* and *B.asiatica*) samples ,but more intense spots were visible in sample A (*B.aristata*) as compare to sample B (*B.asiatica*). The physico-chemical parameters mentioned in the Ayurvedic pharmacopoeia of India is for root and stem of Daruharidra (*Berberis aristata* D.C) in different monographs, are foreign matters, total ash, acid insoluble ash, extractive values etc. Hence, the above mentioned parameters were selected for the analysis of the Ghana tablet. The evolved data will be useful as reference for the analysis of Daruharidra tablet and can be used for its quality control.

Pharmacological Study-

It is quite possible that active principles present in the both Stem Ghana tablet group may produce their anti- hyperglycemic effect through the following mechanisms inhibition glucose absorption, enhancement of peripheral glucose utilization and probably by potentiating the release of insulin from β-cells of langerhans mainly during diet induced hyperglycemic condition. Both drugs did not produce any anti-diabetic activity in alloxan diabetic rats. The exact cause is not known from the available data. However it can be speculated that both the drugs depend upon the availability of endogenous insulin for producing antihyperglycemic activity, because of marked destruction of β-cells during alloxan induction, sufficient amount of insulin is not available for further release by the test drugs.

Histopathological study shows that though the drugs were ineffective in reversing the
diabetes induced hyperglycemia they may be cytoprotective to some of the organs.

Clinical Study:

Majority of the patients were reported in the age group of 41–50 years, This finding is very similar to the latest statistics about Madhumeha which shows that the onset of type–II Diabetes mellitus is in the 40's or 50's, in most of the patients. It is also observed that patients having family history of disease have early onset of disease as compare to the patient having no family history. As B.M.I is concern only 36.11% patients were having normal weight, other was overweight. It is worthful to mention here that that most of patients were having history of weight loss, and they were very obese before onset of disease. After induction of diabetes mellitus patho-physiologically their body weight start reducing as the fats depots are depleted and protein synthesis is prevented this mechanism
helps in improving the condition of patients, these findings also suggest the Dushti of Meda dhatu in Madhumehi patients.

Increased diastolic-systolic blood pressure, increased cholesterol level and obesity indicate that NIDDM is associated with several other disorders such as obesity, hypertension and hyperlipidaemia; this cluster of conditions is specific entity (Syndrome X' or the Metabolic Syndrome) In present study maximum patients were business man; followed by house wife.

Diwasapana, Guru ahara, Snigdha ahara, Ikshu Vikar, Sheeta ahara, Madhura ahara, Drava ahara and Avyayama were other Nidana, It can be concluded from this study that the Kapha-Pitta Karaka ahara and sedentary life style were the most common factors behind the manifestation of this disease as body weight is increased.

In chief complaints, Dourbalyata, Prabhuta Mutrata, Kara-pada-tala-daha was found in maximum patients; it is due to the formation of Ama and mal production of Dhatu. Raised blood Glucose level increases the osmolarity of Glomerular filtrate and thus decreases water absorption as the filtrate passes down the renal tabular system. In this way the volume of urine is markedly increased and Polyuria occurs. This is turn leads to loss of water and mineral which results thirst and Polydipsia. Poor utilization of carbohydrate results in a sense of fatigue.

CONCLUSION

Pharmacognostical study:

Macroscopically both species can be differentiated on the bases of leaves and inflorescence. *B.aristata* leaves spines are not distinct, are glossy green, venation not prominent and corymbose raceme whereas *B.asiatica* leaves spines are distinct, venation prominent and umbellate raceme. Stem is very difficult to differentiate but the yellow intensity of wood is less and bark is more blackish in *B.aristata* as compare to *B.asiatica*. In microscopic study *B.asiatica* can be differentiated by the presence of rhytidoma, starch grains and large vessels which are not present in *B.aristata* however in case of *B.aristata* the prismatic crystal of calcium oxalate are more as compare to former and the medullary rays are wider.

Analytical study

No significant difference was observed in most of the physio-chemical parameters between two drugs Ghana tablets, but the methanol extractive value was about 50% higher in *B.asiatica* as compare to *B.aristata*. The water soluble extractive of stem powder of *Berberis asiatica* (10.70%) was higher as compare to *Berberis aristata* (5.95%).The berberine quantity by Gravimetric method was also higher in case of *Berberis asiatica* stem (0.67%) as compare to *Berberis aristata* stem (0.40%).In TLC also similar spots were seen in both the drugs ghana but the intensity was more in *B.aristata*.

Pharmacological study

In pharmacological studies both drugs are unlikely to cause drug induced hypoglycemia, which is considered as important requisite criteria for the establishment and search of drugs controlling the blood sugar level in diabetic patient. Both the drugs have anti-hyperglycemic effect. The magnitude of this effect is higher in *B.aristata* administered group in comparison to *B. asiatica* administered group. Since both the species did not produce anti-diabetic activity it is doubtful whether they would be useful as main line anti-diabetic drugs. When both drugs are available it should be the *B.aristata* preferred for treating postpranadial hyperglycemic conditions. In case of non-availability of this species *B.asiatica* may be substituted perhaps with higher dose.

Clinical Study

No difference was observed in the therapeutical potential of *Berberis aristata* D.C. and *Berberis asiatica* Roxb.ex.D.C clinically. Both drugs have

highly significant to significant relief in chief complaints and significant relief in postprandial blood sugar level was also seen in both the groups. In *B.aristata* group out of 14 patients, 14.28% patients markedly improved, 57.14% patients improved and 28.57% patients were in unchanged category and in *B.asiatica* group 07.14% patients controled,14.28% patients markedly improved,57.14% improved, and 21.42% in unchanged category. As in pharmacological and Clinical study not much difference is observed in both the drugs, but the water soluble extractive and Berberine quantity is higher in *B.asiatica* groups, so *B.asiatica* can be used in preparation of Rasanjan and other products.

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