Pharmaceutical Standardization

Physico-chemical analysis of a Herbo-mineral compound

Mehamudgara vati – A pilot study

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Abstract

Efforts have been made to lay down analytical standards for Mehamudgara vati (MMV), which were not found reported till date. Weight variation showed that 90% tablets of MMV manufactured in the Gujarat Ayurved University Pharmacy were within acceptable range (323 mg ± 10%), pH 4.58, and disintegration time 17 min, whereas hardness was 1.25 kg/cm². Loss on drying was found to be 9.3% w/w, acid insoluble ash was 0.9 %w/w, water soluble extract was 24.06% w/w and methanol soluble extract 14.1% w/w. Determination of iron as Fe₂O₃ was done as Lauha-bhasma being the major ingredient of MMV. The result showed that iron content was reduced in the formulation (28.67%) as compared to that in Lauha-bhasma (61.19%). In TLC, 5 spots each at 254 nm and 366 nm were found.

Key words: Lauha-bhasma, Mehamudgara vati, standardization, thin layer chromatography

Introduction

Herbal medicines are at great demand globally for primary healthcare due to their higher safety margins and cost effectiveness. Quality control of herbal medicines generates a lot of problems. So first and foremost task is the selection of the right kind of plant material which is therapeutically efficacious compounds. Herbal medicines are being manufactured on large scale where manufacturers face many problems such as low-quality raw material, lack of authentication of raw material, non-availability of standards, lack of proper standardization methodologies of single drugs and formulations and lack of quality control parameters. Classical evaluation of herbal drugs is available based on Rasa, Guna, Virya, Vipaka and Karma etc. In the global view, there is shift towards the use of herbal medicine. At the same time consumers prefer to choose products with established standards. So it is a prime need to standardize Ayurvedic preparations to guarantee their purity, safety, potency and efficacy. Herbal products represent a number of unique problems related to quality which are further complicated by the use of combination of herbal ingredients being used in traditional practice. Therefore, in case of herbal drugs and products the standardization should encompass entire field of study from cultivation of medicinal plant to its clinical application. WHO involves in standardization and quality control of herbal crude drugs[10] to monitor the physicochemical evaluation of crude drugs covering the aspects of selection and handling of crude material, safety, efficacy, stability assessment of finished product, documentation of safety and risk based on experience, provision of product information to consumer and product promotion.

Mehamudgara vati (MMV) is used in the treatment of Prameha, Mutraghata, Mutrakrichchha, Ashmari and Sthula etc.[1] and by analyzing the properties of its ingredients it seems that its use may be justified in these clinical conditions. Till date, no standards are available for Mehamudgara vati. Hence, the present study has been carried out with aims and objectives to develop analytical profile of Mehamudgara vati and by assessing its physico-chemical parameters including weight variation, hardness, disintegration time, pH, loss on drying, ash value, acid insoluble ash, water soluble extract, methanol soluble extract, quantitative estimation of iron content (Fe₂O₃).

Materials and Methods

Before the raw materials used for the preparation of the finished product, proper identification of all plant materials is extremely necessary for its genuineness. This is done by evaluating their quality by various parameters. All ingredients were collected through the Pharmacy of Gujarat Ayurveda University, Jamnagar. Identification of raw drugs was done in Pharmacognosy Laboratory of Institute for Post Graduate Teaching and Research in Ayurveda, where they were proven authenticated as per the standards of Ayurvedic Pharmacopia of India. Firstly, Triphala

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kwatha was made followed by dissolution of Guggulu and Rasanjana in the decoction. All the herbal ingredients were properly mixed with Lauha bhasma. After proper mixing of all the ingredients, they were levigated with Triphala kwatha in end runner and granules were made from the levigated material. After drying of granules, vati were made. Mehamudgara vati contains number of herbs and mineral constituents [Table 1].

Analytical study of Mehamudgara vati was carried out in the pharmaceutical chemistry laboratory of I.P.G.T. and R.A., Jamnagar. Analytical parameters for finished drug were general appearance including size, shape; organoleptic properties; thickness, diameter, hardness, weight variation and disintegration time[8] and physicochemical parameters including loss on drying,[9] ash value, acid insoluble ash,[10] water soluble extractive value and alcohol soluble extractive value[10] and pH[7] Estimation of iron content (Fe$_2$O$_3$)[8] was also done as Lauha bhasma being a major constituent of MMV.

**Determination of Iron (Fe)**

Preparation of sample solution- Required quantity of sample of MMV (in the presence of organic matter) ignited in a crucible furnace at 450-500 C° until the residue becomes free from organic matter. The residue was moistened with 5-10 ml of hydrochloric acid and boiled for 2 min followed by adding 30 ml of water and heating on the water bath for a few min. Then it was filtered and washed thoroughly with water and made up to a volume in a volumetric flask.

**Solutions**

Stannous chloride solution: Dissolve 5 g stannous chloride (A.R) in 25 ml conc. hydrochloric acid and dilute to 100 ml (5% solution). Mercuric chloride: saturated solution in water.

Sulfuric acid + orthophosphoric acid mixture: take 60 ml water, 40 ml conc. sulfuric acid, 30 ml of water and heating on the water bath for a few min. Add 1 ml concentrated hydrochloric acid and boiled for 2 min followed by adding 2-3 drops of diphenylamine barium sulfonate indicator. Then 1-2 ml ammonium chloride was added followed by adding stannous chloride solution drop wise till solution becomes colorless. Then 1-2 drops of stannous chloride solution was added in excess, cooled the content in water and 10-15 ml 10% solution of mercuric chloride was added. A 25 ml acid mixture was taken and 2-3 drops of diphenylamine barium sulfonate indicator was added. Finally, distilled water was added if required and titrated against standard potassium dichromate solution. Appearance of violet color showed the endpoint. Each ml of 1N K$_2$Cr$_2$O$_7$ solution is equivalent to 0.05585 g iron; each ml of IN K$_2$Cr$_2$O$_7$ solution is equivalent to 0.7985 g Fe$_2$O$_3$.

**Observations and Results**

Analytical study of Mehamudgara vati was carried out to establish suitable quality control parameters.

The data of uniformity of tablet shows that 90% tablets were within acceptable range of weight variation [Table 2]. The physicochemical parameters related to Mehamudgara vati and Lauha bhasma are given [Tables 3, 4].

**Table 1: Ingredients of Mehamudgara vati**

| Drug               | Latin name                              | Part used       | Proportion |
|--------------------|-----------------------------------------|-----------------|------------|
| Lauha Bhasma       | Fe$_2$O$_3$                             | Incinerated iron| 15 parts   |
| Guggulu            | Commiphora wightii (Arnott) Wightii      | Exudate         | 4 parts    |
| Haritaki           | Terminalia chebula (Gaerth.) Roxb.      | Pericarp        | 1 part     |
| Bibhitaki          | Terminalia bellerica (Gaerth.) Roxb.    | Pericarp        | 1 part     |
| Amalaki            | Emblica officinalis Gaerth.              | Pericarp        | 1 part     |
| Shunthi            | Zinziber officinalis Rosc.               | Rhizome         | 1 part     |
| Marich             | Piper nigrum Linn.                      | Fruit           | 1 part     |
| Pippali            | Piper longum Linn.                      | Fruit           | 1 part     |
| Trivrita           | Operculina terpethum (Linn) Silva Manso | Root            | 1 part     |
| Pippalimula        | Piper longum Linn.                      | Root            | 1 part     |
| Bida lavana        | –                                       | –               | 1 part     |
| Bilva              | Aegle marmelos (Linn.) Correa           | Fruit           | 1 part     |
| Gokshura           | Tribulus terrestris Linn.               | Seed            | 1 part     |
| Dadima             | Punica granatum Linn.                   | Fruit bark      | 1 part     |
| Devadaru           | Cedrus deodara (Roxb. ex D. Don) G. Don | Heart wood      | 1 part     |
| Rasanjana          | Berberis aristata DC var. aristata      | Extrectum       | 1 part     |
| Kiratatika         | Swertia chirayita (Roxb ex Flem) Karst  | Whole plant     | 1 part     |
| Triphala kwatha    | –                                       | Quantity sufficient for Bhavana |
Table 2: Weight variation test

| Tablet no. | Weight of individual tablet | % weight variation | Tablet no. | Weight of individual tablet | % weight variation |
|------------|-----------------------------|--------------------|------------|-----------------------------|--------------------|
| 1.         | 295 mg                      | 8.67               | 11.        | 322 mg                      | 0.31               |
| 2.         | 348 mg                      | -7.74              | 12.        | 319 mg                      | 1.24               |
| 3.         | 313 mg                      | 3.10               | 13.        | 311 mg                      | 3.72               |
| 4.         | 365 mg                      | -13                | 14.        | 296 mg                      | 8.36               |
| 5.         | 317 mg                      | 1.86               | 15.        | 366 mg                      | -13.31             |
| 6.         | 331 mg                      | -2.48              | 16.        | 323 mg                      | 0.00               |
| 7.         | 302 mg                      | 6.50               | 17.        | 319 mg                      | 1.24               |
| 8.         | 314 mg                      | 2.79               | 18.        | 316 mg                      | 2.17               |
| 9.         | 320 mg                      | 0.93               | 19.        | 350 mg                      | -8.36              |
| 10.        | 355 mg                      | -9.91              | 20.        | 312 mg                      | 3.41               |

Table 3: Result on different quality control parameters

| Parameter                          | Results                        | S.D. | S.E. |
|------------------------------------|--------------------------------|------|------|
| Average weight (uniformity)        | Mean wt. = 324.7 mg; Max. wt= 366 mg; Min. wt= 295 mg | 21.181 | 4.74 |
| Hardness                          | 1.25 kg/cm²                  | 0.38 | 0.09 |
| Disintegration time (water)       | 17 min                       |      |      |
| pH (5% solution)                  | 4.58                          |      |      |
| Loss on drying                    | 9.3% w/w                     |      |      |
| Ash value                         | 45.65% w/w                   |      |      |
| Acid insoluble ash                | 0.9 w/w                      |      |      |
| Water soluble extract             | 24.06 w/v                    |      |      |
| Methanol soluble extract          | 14.1 w/v                     |      |      |
| Iron content (Fe$_2$O$_3$)        | 28.67%                       |      |      |

Table 4: Analytical study on Lauha Bhasma

| Parameter                          | Result |
|------------------------------------|--------|
| Ash value                          | 99.7% w/w |
| Acid insoluble ash                 | 7.9% w/w |
| Iron content (Fe$_2$O$_3$)         | 61.19% |

Table 5: Result of thin layer chromatography

| Sample                | Short UV – 254 nm | Long UV – 366 nm |
|-----------------------|-------------------|------------------|
| Mehamudgara Vati      | Spot no. R$_i$    | Spot no. R$_i$  |
| 1.                    | 0.22              | 1.09             |
| 2.                    | 0.32              | 0.12             |
| 3.                    | 0.67              | 0.32             |
| 4.                    | 0.78              | 0.58             |
| 5.                    | 0.87              | 0.74             |
| 6.                    | 0.83              |                  |

Discussion

In almost all traditional system of medicine, the quality control aspect has been covered by careful observation of skilled physicians. However, in modern concept, it requires necessary changes in their approach by way of quality control in terms of development of modern methodologies. Thus, today quality assurance is a thrust area for the evaluation of traditionally used medicinal plants and herbal formulations. Manufacturers who are doing some testing of their formulation have fixed their own parameter; most of them are only preliminary in nature. Combined and well-coordinated efforts from scientific workers of different disciplines are required for this purpose. Weight variation of tablet causes variation of active medicament which changes the bioavailability. This may be due to causes such as variation in granule size, poor flow, bridging, rat holing, punch variation and poor mixing.

MMV tablets were found to have (mean ± SD) 345.88 mg average weight. 90% tablets were within acceptable range of weight variation as for natural – herbal products, ±10% range of weight variation is acceptable. Both hardness and disintegration time interfere with the bioavailability of drug. MMV was found to have 1.25 kg/cm² hardness and 17 min disintegration time which was noticed with in accepted limits.[9] Moisture content should be minimum to prevent degradation of product. Excess of water in drug encourage microbial growth, presence of fungi or insects and deterioration following hydrolysis. MMV contained 9.3% w/moisture showing that the tablet should be protected from humid atmosphere by keeping silica bag in it as climatic changes affect the tablet. The result shows that if it would not be protected in humid atmosphere, then water activity would be increased and it will cause degradation of the tablet. Ash values are the criteria to judge the identity and purity of crude drug, where total, water soluble and acid insoluble ashes are considered. Mehamudgara vati contained 45.65% w/w of total ash and 0.9% w/w acid insoluble ash. The result revealed that MMV is free from unwanted organic and inorganic compounds and production site was good enough keeping sample free from dust and other soil matters etc. The 24.06%w/w of water soluble and 14.10% w/w of methanol soluble extractive were present in MMV indicating that the drug is having good solubility in water. Though, Mehamudgara vati is prescribed for prameha (type-II
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Sample:
Alcohol extract of MMV

Solvent system:
Petroleum ether (60-80º):
Ethyl acetate: Methanol
(6:2:0.5)

Development:
Stepwise in Stahl chamber

Visualization:
(under U.V. Radiation)
Short U.V. 254 nm,
Long U.V. 366 nm

Figure 1: TLC Profile of Mehamudgara vati (MMV)

Diabetes) in classics, it is indicated in pandu (iron deficiency anaemia) too which is proven in present study by revealing the fact that it contains 28.67% of Fe₂O₃ [Table 3] as Lauha bhasma is the main ingredient of MMV. In TLC of MMV, five spots at 254 nm and six spots at 366 nm were noticed [Table 5 and Figure 1] indicating its possible compounds of the matrix which may possess its therapeutic effect.

Conclusion

The present effort to develop analytical profile of Mehamudgara vati deals with weight variation, hardness, Ph, disintegration time, loss on drying, acid insoluble ash, water soluble extract and methanol soluble extract with determination of iron content in the form of Fe₂O₃ in MMV as well as in lauha bhasma. In TLC, 5 spots at 254 nm and 6 spots at 366 nm were found. This piece of work is just a pilot study which can serve as a preliminary step towards standardization of a herbo-mineral drug Mehamudgara vati. Further study is necessary to explore other parameters related to standardization to be carried out in different batches to set the limit for the reference standards for the quality control and quality assurance of Mehamudgara vati.

References

1. Ritch R. Potential role for Ginkgo biloba extract in the treatment of glaucoma. Med Hypothesis 2000;54:221-35.
2. Bhaisajyagran 37 / 64 – 68 , Kaviyajee Govind Das Sen edited with Siddhiprada Hindi Commentary by Prof. Siddhinandan Mishra. Varanasi: Chaukhambha Sanskrit Sansthan; 2007. p. 703
3. Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. Special indian edition. Bombay: Varghese Publishing House; 2009. p. 299.
4. Anonymous. The Ayurvedic Pharmacopia of India. Part-2, Vol-3, Appendix-3, 1st ed. New Delhi: Ministry of Health and Family Welfare, Government of India; 2010. p. 214 (3.18), 216 (3.19)
5. Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. Special indian edition. Bombay: Varghese Publishing House; 2009. p. 299.
6. Anonymous. The Ayurvedic Pharmacopia of India. Part-2, Vol-1, Appendix -2, 1st ed. New Delhi: Ministry of Health and Family Welfare, Government of India; 2007. p. 141.
7. Anonymous. The Ayurvedic Pharmacopia of India. Part-2, Vol-1, Appendix -3, 1st ed. New Delhi: Ministry of Health and Family Welfare, Government of India; 2007. p. 191.
8. N. Howell Furman. Standard Methods of Chemical Analysis. Vol. I. The Elements, Chap. 25th - Iron: Determination of Iron as Fe₂O₃, Gravimetric method. 6th ed. New York: Krieger Publishing Company, Huntington; 1962, Reprint – 1975. p. 535.
9. Gupta AK. Introduction to Pharmaceutics – I. 3rd ed. New Delhi: CBS Publishers and Distributors; 1994. p. 270.

हिंदी सारांश

हर्बोमिनरल औषधि मेहमुदरावती का भौतिक रासायनिक विश्लेषण – एक प्रारम्भिक अध्ययन

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भौतिक रासायनिक विश्लेषण औषधि के मानकीकरण एवं गुणवत्ता नियंत्रण तथा उत्पादन की गुणवत्ता को सुनिश्चित करने की दिशा में एक महत्वपूर्ण कदम है। आयुर्वैदिक औषधियों का मानकीकरण औषधि की प्राकृतिकता तथा निमित्त कल्प के स्तर पर आयुर्वैदिक वैज्ञानिक गुणवत्ता नियंत्रण प्रक्रिया के माध्यम से किया जाता है। इस अध्ययन में एक शास्त्रीय योगी मेहमुदरावती का फार्मास्यूटिकल विश्लेषण, भौतिक एवं रासायनिक मापदण्डों के आधार पर किया गया है। उक्त वटी का भार 32.3 ग्रा. + 10 %, इला. 4.58, विघटन दर 17 मिनट, कठोरता 9.25 कि.ग्रा. / से.मी. ², शुक्ल होने पर भार में कमी 9.3 % w/w, अम्ल घुलनशील राख 0.9 % w/w, जल घुलनशील सत्र 24.06 % w/w तथा मिश्रितद्राल घुलनशील सत्र 94.1 % w/w पाया गया। प्रेग्लील्ट्रिक धिख से उक्त कल्प एवं लोह भर्म Fe₂O₃ के रूप में उपस्थित लोह की प्रास मात्र से ज्ञात हुआ कि लोह की मात्रा कल्प में (28.67 %), लोहभर्म (61.19 %) की अपेक्षा कम हुई है। औषधि की TLC में 254nm–366nm में 5 चिंड प्रास हुए हैं।