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REVIEW ARTICLE

Critical Review on Pharmaceutical vistas of *Mandura kalpa* (Hematinics of Ayurveda)

Virupaksha Gupta K.L*[1] , Pallavi .G[2] ,Patgiri B.J[1] ,Prashant Math[1]

[1]*Department of Rasa Shastra and Bhaishajya Kalpana including Drug Research, IPGT and RA, Gujarat Ayurved University, Jamnagar, Gujarat, India*
[2]*Department of Basic Principles, Government Ayurveda Medical College, Mysore, Karnataka, India*

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ABSTRACT

Iron is an essential trace metal in the human body. Its inadequacy leads to Iron Deficiency Anemia. Contemporary medical science prescribes ferrous salts for the treatment of anemia. These tend to induce some adverse effects. Hence, Mandura Kalpas are an alternative and are noteworthy iron formulations of Ayurveda. Literary search of different Ayurvedic Classics (Bhaishajya Ratnavali, Charaka Samhita, Ashtanga Hridaya, Chakradatta etc.) reveals many Mandura Kalpas which are found to be therapeutically significant. Most of the formulations are prepared by Rasakriya method and few of them by Khalviya and other methods. Many of the formulations are processed in cow urine. Hence some beneficial role of cow urine in the iron metabolism has been anticipated. This study critically review's the Mandura kalpas (Hematinics) of Ayurveda and it also identifies the need for further research on the role of cow urine in iron metabolism.

Key words: *Mandura kalpa*, Rasakriya method, Khalviya, Cow urine.

INTRODUCTION

Ayurveda is an inspiration for contemporary researchers to think beyond their knowledge and imagination. It is also applicable to the pharmaceutics of Ayurvedic medicine. Careful insights into the classical texts of Ayurveda reveal innumerable formulations of different dosage forms in different ailments. The underlying reasons for using herbs and minerals are not completely known even today. For example repeated observations made by earlier scholars on the presence of *Trikatu* in most of the Ayurvedic formulations lead to the invention of bio-enhancing property of piperine.[1] Hence if research is undertaken in reviewing, classifying and critically analyzing all the formulations some out puts can be anticipated.

Pharmaceutics of Ayurveda can be broadly classified into Mineral Pharmaceutics of Indian Medicine (MPIM, *Rasa Shastra*) and Herbal Pharmaceutics of Indian medicine (HPIM, *Bhaishajya Kalpana*). There are different types of dosage forms where in the presence of various ingredients repeated regularly can reveal some details regarding their rationality . In line to it, one major metal i.e. iron containing *Mandura* formulations are reviewed.

Background: Iron deficiency anemia is a common problem in the developing countries like India. The treatment of iron deficiency anemia in the contemporary science with iron salt preparations like ferrous sulfate results in several adverse effects viz. severe gastrointestinal irritation, necrosis of the mucous membrane, cardiovascular collapse; severe damage to brain and liver or even death might occur.[2] It is need of the hour to search some better alternative, as hematinics market is hopping around 9000 million rupees and growing at 15% per annum.[3] Safe effective formulations can certainly become a boon. *Mandura Kalpas* are the promising iron containing herbomineral formulations of Ayurveda. Till date no evident scientific comprehensive review has been done on *Mandura Kalpas* in Pharmaceutical aspect. Hence this study is undertaken.

Some Researches have been carried out on individual *Mandura Kalpas* like *Punarnavadi Mandura*[4], *Satavari Mandura* [5,6], *Trayushanadi Mandura*[7], *Koladi Mandura*,[8,9] *Kshira Mandura*, [10] *Vajra Vataka Mandura*[11]

Description of *Mandura*: *Mandura* is the debris accumulated around the anvil of blacksmith during the heating and beating process of Iron.

***Corresponding Author:** Dr.Virupaksha Gupta K.L, **Email:** virupakshgupta@gmail.com

Mandura is collected from the respective sources like age old anvils and abandoned towns, considered to be very useful, if they are about 100 years old. The samples of 80 years and 60 years old are considered as moderate and comparatively less effective for therapeutic purposes. Chemically, *Mandura* is the combination of Ferric Oxide (59.14%), Ferrous Oxide (26.7%), Chlorides (4.4%), Magnesium (3.9%), Sodium (1.7%) and few other trace elements, Purification (Shodhana) of Mandura should be carried out by heating and quenching (Nirvapa) in cow urine seven times.

Brief Description of *Mandura Kalpa* [12]

Definition:

These are preparations containing *Shodhita Mandura* along with other drugs.

Method of preparation:

Shodhita Mandura should be boiled in Cow urine till it becomes a *Rasakriya* (a paste). Then other ingredients of the formulation are added and stirred well. *Vatakas* are prepared when the mixture is still warm. This can be used in powder form also.

Characteristics and preservation:

These emit a strong smell of Cow urine and are dark in colour. These preserve their potency for ten years. Mercury containing Preparations keep their potency indefinitely. [13] These should be kept away from moisture.

Different Methods of Preparation:

Important texts of Ayurveda such as *Charaka Samhita* (CS), *Chakradatta*, and *Bhaishajya Ratnavali* (BR) have been the sources for *Mandura Kalpas* and they are enumerated according to the method of preparation. The formulations having suffix as *Mandura* are only considered for the study. The other *Mandura* containing dosage forms are excluded from the study.

Quantity of *Mandura* in few formulations is quoted as '*Sarva dravya samam'* which means 50% of the formulation will be *Mandura Bhasma.* In other formulations the quantity is calculated in accordance with the solid constituents, where in the ingredients like decoctions (*Kwatha*), fresh juices (*Swarasa*), ghee (*Ghrita*, clarified butter) and Honey (*Madhu*) are not taken into consideration(unless specified). Calculation is based on the ingredients taken prior to the preparation. Hence percentage in final product will change except in *Churnas*. Percentage is not mentioned in the formulations where no other solid constituents are present.

Method of calculation:- Percentage of *MB* =100×Weight of *MB*/Weight of total solid constituents.

Mandura Rasakriya kalpa [14]**:**

The formulation prepared by the boiling of Primary liquid dosage forms till the attainment of semisolid consistency is known as *Rasakriya*.

Here *Mandura Bhasma* is boiled along with different herbal juices and decoctions until it converts to semisolid dosage form. But *MB* and Cow urine (eight times to the *MB*) are boiled in most of the formulations and in few with specified herbal decoctions up to the semisolid consistency and rolled into pills after addition of the powders of *Prakshepa Dravyas.*

Table no. 1 Formulations Prepared by *Rasakriya*

S. No	Name of the formulation	Mineral ingredient	Herbal ingredient	Processing Drugs
1.	*Mandura Vataka*- 1[15]*Δ	*MB* (67%), *SMB*	*Trikatraya, Chavya, Devadaru, Pippalimula, Darvi*	Cow urine
2.	*Mandura Vataka-2* [16]	*MB* (67%)	*Trikatraya, Chavya Devadaru, Kutaja*	Cow urine
3.	*Mandura Vataka-3*[17] Δ	*MB* (67%), *SMB.*	*Daruharidra, Twak, Chavya, Granthika, Devadaru, Trikatu*	Cow Urine
4.	*Vajra Vataka Mandura*[18]	*MB* (67%)	*Trikatraya, Chavya, Devadaru, Pippalimula*	Cow urine
5.	*Triphaladi Mandura*[19]*	*MB* (50%)	*Trikatraya, Chaturjata, Kalajaji, Ajamoda, Yashti, Dhanyaka*	*Triphala, Guduchi, Bhringaraja, Kesharaja, Vasa, Shatavari, Mundi, Bala, Patola, Parpata, Bharangi, Kirata, Neeli, Brahmi Swarasa's*
6.	*Punarnavadi Mandura*[20]*Δ	*MB* (67%)	*Punarnava, Trivrit, Trikatraya, Ushana, Pippalimula, Chavya, Chitraka, Devadaru, Pushkara, Katuki, Indrayava, Haridra, Darvi*	Cow urine
7.	*Thrayushanadi Mandura*[21]	*MB* (67%), *SMB*	*Trikatraya, Chavya, Darvi, Dalchini, Pippalimula, Devadaru*	Cow urine
8.	*Koladi Mandura*[22]	*MB* (50%), *YK*	*Chavya, Pippalimula, Shunti, Pippali*	Cow urine

9.	*Punarnavadi Mandura*[23]*	*MB* (67%)	*Punarnava, Trivrit, Trikatraya, Ushana, Pippalimula, Chavya, Chitraka, Devadaru, Pushkara, Katuki, Indrayava, Haridra, Darvi*	Cow urine
10.	*Bhima vataka Mandura*[24]	*MB* (76%), *YK*	*Chavya, Pippalimula, Shunti, Pippali*	Cow urine
11	*Kshira Mandura*[25]	*MB*	Nil	Cow urine, Cow milk
12.	*Thara Mandura*[26]*	*MB* (50%)	*Trikatu, Triphala, Vidanga, Chitraka, Chavya, Haritaki, Amalaki, Guda*	Cow urine
13.	*Agnimukha Mandura*[27]	*MB* (46%)	*Pancha Kola, Devadaru, Mustha, Vidanga, Triphala*	Cow urine
14.	*Amritadi Mandura*[28]	*MB* (67%)	*Guduchi, Nimbha, Bhunimbha, Brihati, Pippali, Haridra, Yashti, Murva, Manjishta, Satavari, Lavanga, Patala, Jala Pippali,*	Cow urine
15.	*Bhima vataka Mandura*[29]	*MB (76%), YK*	*Chavya, Pippalimula, Shunti, Pippali*	Cow urine
16	*Panchamrita Lauha Mandura*[30]	*MB* (34%), *LB, TB, Kajjali, AB*	*Kirata tikta, Devadaru, Haridra, Darvi, Pushkara, Yavani, Shwetajeeraka, Krishnajeeraka, Shathi, Dhanyaka, Chavya*	Cow urine, *Punarnava*, Honey
17	*Shothari Mandura*[31]*	*MB* (67%)	*Triphala, Trikatu, Chavya*	*Nirgundi, Manakanda, Ardraka, Surana Kanda Swarasa, Triphala, Trikatu, Chavya Kwatha- Bhavana* Cow urine – *Kwathana (Boiling)*
18	*Sita Mandura*[32]	*MB* (27%)	*Triphala, Trikatu, Ela, Duralabha, Vidanga, Kushtha, Lavanga*	Sugar, Cow milk, Honey, Cow ghee
19.	*Shatavari Mandura*[33]	*MB* (50%)	*Shatavari*	*Shatavari Swarasa*, Curd, Cow milk
20	*Shatavari Mandura (brihat-1)*[34]	*MB*	*Jiraka, Musta, Dhanyaka, Trijata*	*Shatavari Swarasa, Amalaki Swarasa*, Cow milk, Cow ghee, Curd
21	*Shatavari Mandura (brihat-2)*[35]	*MB* (53%), *LB, AB*	*Vidanga, Triphala, Trikatu, Jeeraka Dwaya, Yavani, Gaja Pippali, Musta*	*Shatavari Swarasa, Amalaki Swarasa*, Cow urine, goat milk, Sugar candy, Cow ghee,
22.	*Rama Mandura*[36]	*MB* (20%)	*Vasheeram, Shweta Vatyala, Guduchi, Apamarga, Tanduliyaka*	Cow's urine, Jaggery

***Khalviya Lauha Kalpa*:**

Herbal juices are added to the metals and minerals (*Bhasma)*, then triturated till the liquid portion is totally dried. The liquid added should be of optimum proportion, by which it gets sufficient moisture to form soft or soggy mass [37].

Table 2: Khalviya formulations

S.No	Name of the formulation	Mineral ingredients	Herbal ingredients	Processing Drugs
1.	*Takra Mandura-1*[38]	*MB* (10%), *Samudra phena, Saindhava Lavana*	*Vijaya, Vamsa, Kaliyaka (Kala Agar) Nimba, Vishatinduka Mula, Tejpatra, Lavanga, Ela, Shatapushpa, Madhurika, Maricha, Guduchi, Yasti, Jayapala, Shunti*	*Punarnava Swarasa*
2.	*Takra Mandura-2*[39]	*MB*	Nil	*Bilva Patra, Shweta* and *Krishna Bhringaraja, Agnimantha, Punarnava, Kokilaksha Swarasa*, Cow urine
3.	*Chatuhsama Mandura*[40]	*MB* (25%)	Nil	Sugar, Honey, Cow ghee,
4.	*Guda Mandura*[41]	*MB* (50%)	*Amalaki, Haritaki*	Old Jaggery, Honey, Cow ghee
5.	*Mandura Vataka*[42]	*MB* (67%), *SMB*	*Trikatu, Devadaru, Chitraka, Sandhalu, Ardhraka, Bringaraja*	Cow urine
6.	*Thapyadi Mandura*[43]	*MB* (20%), *Shilajit, SMB, RB*	*Triphala, Trikatu, Chitramula, Vidanga,*	Sugar, Honey
7.	*Rasabhra Mandura* [44]	*Kajjali, AB, MB* (34%), *Shilajit, KLB*	*Trikatu, Triphala, Chavya, Musta*	*Bhringaraja, Kesharaja, Nirgundi Kwatha, Manakanda, Ardraka Swarasa*
8.	*Rasa Mandura*[45]	*Kajjali, MB* (24%)	*Haritaki*	*Bhringaraja, Kesharaja Swarasa*, unequal Parts of Honey, Cow ghee

Table 3: Miscellaneous preparations and their method of preparation

Method of preparation	Name of the formulation	Mineral ingredients	Herbal ingredients	Processing Drugs
Churna	*Triphala Mandura*[46]	*MB* (50%)	*Triphala*	Nil
Puta Paka	*Trikatwaradi Mandura*[47]	*MB* (50%), LB (2.6%)	*Trikatu, Triphala, Draksha, Pushkara, Shati, Vacha, Lavanga, Shringi, Tvak, Shatapushpa, Vibhitaki, Vidanga, Dhataki Pushpa Kutaja Kwatha*	*GAJAPUTA*

*- Formulations mentioned in AFI part 1&2

Δ- Formulations available in Market (Ayurvedline)

Abbreviations & Important Terms

LB**-Lauha* (iron or steel) *Bhasma; **KLB**-Kanta Lauha* (magnetite or lode stone) *Bhasma; **MB**-Mandura* (iron rust) *Bhasma* ***RB**-Rajata* (Silver) *Bhasma; **VB**-Vanga* (Tin) *Bhasma*); SMB**-Swarna Makshika* (copper pyrite) *Bhasma*

Trika Traya: formulation possessing *Triphala, Trikatu, Trimada; **AB**-Abhraka* (Biotite mica) *Bhasma*; ***TB**-Tamra* (copper) *Bhasma*; ***YK**-Yava Kshara*

DISCUSSION:

Ayurveda is the distilled core of knowledge obtained after centuries of trial and experimentation of ancient seers. Ancient seers achieved excellence in all aspects including Pharmaceutics. A recent review showed that more than 13,000 plants have been investigated during the past 5 years.[48] But unfortunately therapeutic potentials of metals and minerals were ignored by the scientific community which may be due to concerns of safety. But Ayurveda has never neglected these novel elements. *Rasa Shastra* explains the conversion of these into consumable form. Iron is a metal used by the modern science since a long in the form of ferrous salts for iron deficiency anemia. *Mandura* (iron rust) has been used since *Samhita* period in Ayurveda.

Regarding administration of Iron, versatility can be found in terms of *Mandura Kalpa and Lauha Kalpa.* Therapeutic utilization of *Mandura* is mentioned in *Charaka Samhita* but systematic and extensive use has been elaborated in *Rasa Granthas*. Careful observation of *Mandura Kalpas* reveals that these are not only used in *Pandu* (Iron Deficiency Anemia) but also in wide range of clinical conditions like *Shula* (Gastritic pain due APDs), *Shotha* (edema), *Amla Pitta* (Hyperacidity). Incineration (*Bhasmikarana*) of *Mandura* is not explained in most of the ancient *Rasa* literature. Earlier texts considered *Shodhita Mandura* for the preparation of *MKs*. It is in *Rasa Tarangini* for the first time the incineration process is explained. Hence ambiguity arises in the use of *MB*. But after considering the advantages of Puta[49] such as light for digestion (*Laghutwam*), fast absorption (*Sheeghra vyapti*), enhances digestive fire (*Deepanam*), Mandura Bhasma is considered ideal than *Shodhita mandura*.

Experimental Studies on its Gastro intestinal tolerability and Hepato-protective property of MKs: Some studies shows that simultaneous treatment with *Mandura Bhasma* prevented the paraffin mediated and $CC1_4$ mediated changes in the enzyme activities. These results suggest the hepatoprotective role of *Mandura Bhasma* during $CC1_4$ induced hepatic injury.[50] *Lauha Bhasma* and *Mandura Bhasma* in 55 mg/kg dose (5 times the therapeutic effective dose) for 60 days exhibited no serious toxic effects in Charles Foster albino rats. Both the drugs showed significant recovery from chronic toxic effect after 45 days of recovery period.[51]

Shatavari Mandura is described in *Shula* vis-à-vis Peptic Ulcer Syndrome. When administered it in a dose of 125-500 mg/kg orally, twice daily for three, five and seven days showed protective effect in cold restraint stress-induced gastric ulcer in rats. The effective regimen was found to be 250 mg/kg, given for five days. Hence was used for further experiments. It showed significant protection against acute gastric ulcers induced by pyloric ligation but was ineffective against aspirin- and ethanol-induced ulcers. Further, gastric juice studies showed that, it significantly increased the mucosal defensive factors like mucus secretion, but had little or no effect on offensive factors like acid and pepsin secretion.[52] It shows that the MKs instead of causing Gastric irritation like contemporary ferrous salts these are gastro-protective and hepatoprotective. Hence there is lot of possibility of public acceptance once if these noble formulations are scientifically validated.

Nomenclature:

Based on quantity of ingredients - *Chatuhsama Mandura*

Based on the *Bhavana Dravya* - *Shatavari Mandura*, *Kshira Mandura*

Based on sweetening agent – *Guda Mandura, Sita Mandura*

Based on another mineral ingredient - *Rasa Mandura, Rasabhra Mandura*

Based on Herbal ingredients - *Triphala Mandura*

Based on *Pathya* - *Takra Mandura* (*Takra*, buttermilk) here *Takra* is not an ingredient in any

of these preparations, but should be consumed as regular diet instead of water and salt.)

Role of *Gomutra* (cow urine): Among two third formulations of total MKs cow urine is the one used mostly. Cow urine was patented (U.S. Patents No.6896907 and 6,410,059) for its medicinal properties recently, particularly for its use along with antibiotics for the control of bacterial infection and fight against cancers. [53] One study supports the fact about traditional use of *Gomutra Arka* for immuno-modulatory and antioxidant effect. [54] Although there are claims about the enhancement of antioxidant enzymes by Cows urine but the fact is yet to be supported by scientific studies [55]. Cow urine is a proved bio enhancer [53]. Hence the role of cow urine is highly justified. But till date no evident study has been done on validating the bio enhancing property of cow urine on iron .Hence further researches can be planned to validate it.

But MKs emits strong smell of cow urine, making it unpalatable which probably will be the limiting factor for its administration in some patients. Hence by using the advancements of Pharmaceutical technology it will be wise to modify the dosage form as encapsulated or enteric coated.

Weight changes:

Documentation of weight changes are essential part for the drug standardization. Assessment of final weight in relation to initial weight will give pharmacist an idea to choose the weight of ingredients according to the requirement.

Cow urine consists of 2.75 - 3% solid content; hence up to 24% weight of *MB* will certainly increase the final weight as cow urine is used eight times to the quantity of *MB*.

In the preparation of *Punarnavadi Mandura* initial weight of all ingredients were 30 kg (20 kg *MB*, 10 kg herbal ingredients), finally 30.72 kg final product with 6.8% loss on drying was observed, which indicates 7.2 kg (24% to total wt, 34% to *MB*) weight gain.[56] Here in 34% of weight gain, up to 24% is due to cow urine and 4% to 10% is due to moisture content as loss on drying observed was 6.8%.

In pharmaceutical study of *Kshira Mandura* it is observed that if initial weight of 800 gm of *MB* was taken for the study, 920 gm of final product was obtained i.e. weight gain of 120 gm was observed. (16.5%).[57]

Takra Mandura (S.No.2 in Table 2) is prepared by *Khalviya* method, when it is prepared with 1250 g. *MB* gave yield of 1410 gm of final product which indicates 240 g. weight gain is 18 %.[58]

Administration of *Mandura Bhasma* alone or in compound form is very rational since centuries. PRAK 20 (ethical version of *Punarnavadi Mandura*) has shown potent hepato-protective, anti-fibrotic, anti-inflammatory, detoxifying and anti viral properties in various pre-clinical and clinical studies. [59]

One study identifies the necessity of further studies to understand the complexity of daily dose schedule and to rationalize Minimum Required Dose (MRD) and Maximum Tolerant Dose (MTD) of *Mandura* [60]

CONCLUSION

Mandura Kalpas are the promising answer for the search of safe and effective Iron preparations. They can be safer and more acceptable than the present day hematinics of modern medicine. Some *Mandura Kalpas* are indicated in Acid Peptic disorders implicating more gastric safety. Regarding the method of preparation most of the MKs is prepared by *Rasakriya* method. But there are few preparations prepared according to *Khalviya* method. MKs are solid dosage forms, but few are in semisolid dosage form because of the addition of Ghee and Honey. Cow urine plays a vital role in the preparation of *Mandura Kalpa*. The bio-enhancing property of cow urine in ADME of Iron has to be ascertained by further research. This research may pave way for the further researches on *Mandura kalpa*.

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