



AN APPRAISAL OF THERAPEUTIC IMPLICATIONS OF UNMADA GAJA KESARI RASA IN VARIOUS NEUROPSYCHIATRIC DISORDERS

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ABSTRACT:

Unmada Gaja Kesari Rasa is a traditional herbo-mineral compound cited in the lexicon of the 15th century AD. As the name suggests, it is commonly prescribed in *Unmada* (psychosis). The classics also recommend its use in *Apasmara* (epilepsy) and other psychiatric conditions, such as *Jwara* (Syndrome/fever) and *Bhootonmada* (insanity due to possession). The standard antipsychotics pose adverse effects that may substantially affect the quality of life of psychiatric patients. Therefore, there is a need to explore the novel drug in the management of psychotic diseases. In Ayurveda, psychiatric disorders are referred to as *Unmada*, and the line of management of *Unmada* has proven to be beneficial in various psychiatric conditions such as MDD, Schizophrenia, etc. Unmada Gaja Kesari Rasa is the first drug of choice in *Unmada*. Therefore, we planned to study the formulation, its variations in composition, dose, adjuvant, therapeutic utility, and method of preparation. As the formulation contains a potent toxic drug, we also studied its toxicity profile. Citations of relevant studies have been enumerated.

Key words: Unmada, Unmada Gaja Kesari Rasa, Unmadgaja Kesar Rasa, Antipsychotic, Antidepressant, Anticonvulsant, Ayurveda

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INTRODUCTION

Unmada Chikitsa Adhikara is the chapter of reference for all neuropsychiatric disorders and psychological abnormalities in Ayurveda. Unmada is often correlated with schizophrenia, mood disorder with psychosis, substance abuse-induced psychosis, etc. The therapeutic guidelines primarily include *Samshodhana karma* (the bio-cleansing therapy). Various herbal, herbal-mineral, and lipid-based medicines are used according to the severity of the illness [1]. *Unmada Gaja Kesari* Rasa is a herbo-mineral formulation aimed to treat various psychiatric illnesses such as *Unmada*, *Apasmara*, and *Bhootonmada* [2]. Clinically, the formulation is indicated in various psychiatric abnormalities such as *Manodukhaja unmada* (*unmada* due to lack of happiness), MDD, schizophrenia, bipolar disorder, etc. This claim has been supported by experimental studies and validates age-old therapeutic principles. As herbo-mineral formulations act quickly and are effective in small doses, they are commonly used in clinical practise. In the classics, various references with diverse methods of preparation and composition are available. Therefore, to understand the therapeutic efficacy, dose, effective adjuvant an attempt is made to review the compositions, and experimental validation of

different types of *Unmada Gaja Kesari Rasa* in various neuropsychiatric disorder.

METHODS

A manual review was conducted of relevant literature found from the database searches and also of Ayurveda classical texts. The search was carried out using the key words "*Unmada Gaja Kesari Rasa*", "*Unmadgaja Kesari Rasa*", "*Unmadgajakesari Rasa*", *UGK*, *Dhatura*, *Gandhaka*, *Parada*, *Vacha*, *Brahmi*, *Shankhapushpi*, *Gomutra*, and *Bhavana*. The studies conducted on *Unmada Gaja Kesari Rasa* were included in the manuscript. The manuscript was prepared by highlighting varieties of *Unmada Gaja Kesari Rasa* and its therapeutic profile.

RESULTS AND DISCUSSION

On meticulous screening and extracting relevant data from electronic media and classical textbook, seven varieties of preparation were selected for the study. The review revealed that *Kajjali* was present in all the preparations. *Shudha Parada* (purified mercury), *Shudha Gandhaka* (purified sulphur), *Shudha Manashila* (purified realgar), and *Dhatura beeja* were the commonest ingredients in *Unmada Gaja Kesari Rasa*. The common *Anupana* (Adjuvant) mentioned was *Ghrita* (Clarified butter) and the dosage prescribed was 1 *Masha* (1 gm). The formulation was studied to be effective in low

dose in an animal model. Pharmaceutically, the formulation is prepared with a variety of ingredients, different methods of preparation, and diverse references in classics. Drug combinations are intended to serve a variety of functions, including synergistic actions, combined actions, toxicity neutralisation actions, and individualised actions. Over-all, *Unmada Gaja Kesari* contains *Shudha*

Gandhaka, Shudha Parada, Shudha Manashila, Shudha Vatsanabha (purified aconitum), *Shankhapushpi, Vacha, Brahmi, Dhatura seeds, Rasna, Gomutra, Tamra bhasma, Abhraka Bhasma, Kupeelu, and Agastya*. The compositions of different references of *Unmada Gaja Kesari Rasa* mentioned in classical texts have been depicted in Tables 1–7.

Table 1: Unmada Gaja Kesari Rasa 1(a)

Unmada Gaja Kesari Rasa I (a)	
Ingredients	<ol style="list-style-type: none"> 1. <i>Shodhita Parada</i> (Mercury) 2. <i>Shodhita Gandhaka</i> (Sulphur) 3. <i>Shodhita Manahshila</i> (Realgar) 4. <i>Shodhita Dhatura seeds</i> (<i>Dhatura metel</i>) <p style="text-align: right;">} all in equal parts</p>
<i>Bhavana dravya</i>	7 <i>bhavana</i> (trituration) with decoction of <i>Vacha</i> (<i>Acorus calamus</i>) + <i>Brahmi</i> (<i>Bacopa monnieri</i>) <i>swarasa</i> (juice)
Dose	1 <i>Masha</i> (1 gm)
<i>Anupana</i> (Adjuvant)	<i>Ghrita</i>
Indication	<i>Unmada, Apasmara, Bhutonmada, Jwara, Anidra</i>
Reference	<i>Bhaishajya Ratnavali Unmada adhikara</i> ^[2]

Table 2: Unmada Gaja Kesari Rasa 1 (b)

Unmada Gaja Kesari Rasa I (b)	
Ingredients	<ol style="list-style-type: none"> 1. <i>Shodhita Parada</i> (Mercury) 2. <i>Shodhita Gandhaka</i> (Sulphur) 3. <i>Shodhita Manahshila</i> (Realgar) 4. <i>Shodhita Dhatura seeds</i> (<i>Dhatura metel</i>) – 3 parts <p style="text-align: right;">} 1 part</p>
<i>Bhavana dravya</i>	7 <i>bhavana</i> (trituration) with decoction of <i>Vacha</i> (<i>Acorus calamus</i>) + <i>Brahmi</i> (<i>Bacopa monnieri</i>) <i>swarasa</i> (juice)

Dose	1 Masha (1gm)
Anupana (Adjuvant)	Ghrita
Indication	Unmada, Apasmara, Bhutonmada, Jwara
Reference	Brihat Rasaraj Sundar ^[3]

Table 3: Unmada Gaja Kesari Rasa 1 (c)

Unmada Gaja Kesari Rasa I (c)	
Ingredients	<ol style="list-style-type: none"> 1. Shodhita Parada (Mercury) 2. Shodhita Gandhaka (Sulphur) 3. Shodhita Manahshila (Realgar) 4. Shodhita Dhattura seeds (<i>Dhatura metel</i>)
Bhavana dravya	7 bhavana (trituration) with decoction of Vacha (<i>Acorus calamus</i>) + Rasna (<i>Pluchea lanceolata</i>)
Dose	1 Masha (1gm)
Anupana (Adjuvant)	Ghrita
Indication	Unmada, Apasmara, Bhutonmada, Jwara
Reference	Yoga Ratnakara Unmada chikitsa ^[4]

Table 4: Unmada Gaja Kesari Rasa 1 (d)

Unmada Gaja Kesari Rasa I (d)	
Ingredients	<ol style="list-style-type: none"> 1. Shodhita Parada (Mercury) 2. Shodhita Gandhaka (Sulphur) 3. Shodhita Manahshila (Realgar) 4. Shodhita Dhattura seeds (<i>Dhatura metel</i>)
Bhavana dravya	7 bhavana (trituration) with decoction of Vacha (<i>Acorus calamus</i>) + Agastya (<i>Sesbania grandiflora</i>) + Brahmi (<i>Bacopa monnieri</i>) swarasa (juice)
Dose	1 Masha (1gm)
Anupana (Adjuvant)	Ghrita

Indication	<i>Unmada, Apasmara</i>
Reference	<i>Rasa chanamshu Unmada chikitsa</i> ^[5]

Table 5: Unmada Gaja Kesari Rasa 2 (a)

Unmada Gaja Kesari Rasa II (a) ^[6]	
Ingredients	1. <i>Shodhita Parada</i> (Mercury) 2. <i>Shodhita Gandhaka</i> (Sulphur)
<i>Bhavana dravya</i>	7 <i>bhavana</i> (trituration) with decoction of <i>Vacha</i> (<i>Acorus calamus</i>) + 3 trituration with <i>Shankhapushpi swarasa</i> (<i>Convolvulus pluricaulis</i>) <i>Bhavana</i> with <i>Gomutra</i> (cow urine)
Dose	12 ratti
<i>Anupana</i> (Adjuvant)	<i>Goghrita</i> and <i>Sarshapa choorna</i> in equal quantity
Indication	<i>Unmada, Apasmara</i>
Reference	<i>Rasa Sanket Kalika</i> <i>Rasa Kamadhenu</i>

Table 6: Unmada Gaja Kesari Rasa 2 (b)

Unmada Gaja Kesari Rasa II (b)	
Ingredients	1. <i>Shodhita Parada</i> (Mercury) 2. <i>Shodhita Gandhaka</i> (Sulphur)
<i>Bhavana dravya</i>	Trituration of <i>Shudha Parada</i> with <i>Vacha Kwatha</i> and equal parts of <i>Shudha gandhaka</i> with <i>Shankhapushpi swarasa</i> for 3 days. Triturated <i>Shudha parada</i> and <i>Gandhaka</i> is mixed with <i>Gomutra</i> .
Dose	1 <i>Masha</i> (mixed with equal parts of <i>Sarshapa Choorna</i>)
<i>Anupana</i> (Adjuvant)	<i>Jeerna ghrita</i>
Indication	<i>Unmada, Apasmara</i>
Reference	<i>Brihat Bhisajya Ratnakara</i> ^[7]

Table 7: Unmada Gaja Kesari Rasa 3

Unmada Gaja Kesari Rasa III ^[6]	
Ingredients	<ol style="list-style-type: none"> 1. <i>Shodhita Parada</i> (Mercury) 2. <i>Shodhita Gandhaka</i> (Sulphur) 3. <i>Shodhita Dhatura</i> seeds (<i>Datura metel</i>) 4. <i>Tamra Bhasma</i> 5. <i>Abhraka Bhasma</i> 6. <i>Shodhita Vatsanabha</i>
<i>Bhavana dravya</i>	7 <i>bhavana</i> (trituration) with juices of <i>Datura</i> , <i>Kupeelu</i> (<i>Strychnos nuxvomica</i>) and <i>Maharashtri</i> (<i>Argemone mexicana</i>)
Dose	3 <i>ratti</i> (375mg)
<i>Anupana</i> (Adjuvant)	<i>Madhu</i> and <i>Vacha Kwatha</i>
Reference	<i>Rasa Raj Sundar</i> <i>Rasa Chandanshu</i> <i>Rasa Kamdhenu</i> <i>Rasendra Sara Sangrah</i> <i>Bhaishajya Ratnawali</i> <i>Rasendra Chintamani</i> <i>Rasendra Kalpadrum</i>

Therapeutic profile of Unmada Gaja Kesari Rasa

Shodhita Gandhaka is *Rasayani* ^[8] (rejuvenating) and it is indicated in *chittavibhrama* (instability of mind) along with other pharmacological properties ^[9]. *Gandhaka* is extremely *Deepana* (digestion enhancing), so it may kindle the digestive fire and remove *sroto avarana* (clears the obstructive pathology occurring in channels)

^[9]. *Shudha Parada* is *tridosahara* (balances three regulatory functional factors of the body) and possess *Rasayana* property. Mercury crosses blood brain barrier, deposits in the brain thus alter multiple cellular functioning ^[10]. *Kajjali* is a combination of *Parada*, *Gandhaka* and contains a unique property called as *yogavahi* (carrier of properties). This property of *Kajjali* assists in transporting other medications to the central

nervous system and increase the efficacy and potency of the formulation.

Shudha Manashila is an arsenic compound, has been extensively used in several formulations in Ayurveda. It was indicated in *Bhaya* (phobic disorders), *Bhootavesha* (possession of bhoota), *Apasmara*. In Raja Nighantu, *Manashila* is mentioned under Unmada Adhikara as *Vashyakarini* (Hypnotic). Realgar was used as sedative in chine traditional medical system. It acts as CNS depressant by potentiating the activity of GABA [11]. *Dhatura (Dattura metel)* exhibits strong antidepressant properties. The plant contains scopolamine, a strong cholinergic-blocking hallucinogen [12]. Hyoscyamine and atropine found in its leaves make them a potent source of anticholinergics [13]. Along with anti-cholinergic, *Dhatura* is also a potent sedative.

Vacha- In *Unmada chikitsa*, *Vacha* is an essential drug of choice. It is *Kapha Vatahara* (normalising vata and Kapha dosha), *srotoshodhana*, *deepana-pachana* (digestion and metabolism enhancing), *Medhya* (intellect enhancer) and *Vatanulomana* (proper functioning of vāyu) in nature [1]. *Acrous calamus rhizomes'* methanolic extract exhibits antidepressant effect, which is likely due to interactions with the adrenergic, dopaminergic, serotonergic, and gamma-

aminobutyric acid (GABA)nergic systems [14]. It has been demonstrated that the mice models are equally useful for demonstrating compounds with potential antidepressant action [15]. *Vacha* also exhibits neuromodulatory effects on nigrostriatal dopaminergic system, GABAergic actions along with antioxidant and neuroprotective activity [16]. Flavanoids in *vacha* crosses blood brain barrier and acts as MAO inhibitor [17].

Rasna- *Taraxasterol* and its naturally occurring acetate counterpart from *Pluchea lanceolata* inhibit the release of TNF-, IFN-, and IL-6 in the rat astrocytoma cell line (C6), protecting against neuroinflammation. According to the study, *taraxasterol* inhibited LPS-induced neuroinflammation effectively, most likely through the activation of the NF- κ B and *taraxasterol* acetate by TNF- pathways [18].

Brahmi- *Bacosides* are a type of naturally occurring phytonutrient found in *brahmi*. This enhances crucial neurotransmitter functions involved in memory and information processing and may be beneficial for depression [19]. According to experimental data, *Bacopa monnieri* Linn likely has strong antidepressant properties. *Brahmi* was also studied to have an add on effect in schizophrenia [20]. GABAergic actions along with antioxidant and neuroprotective activity [21].

Shankhapushpi- Alkaloids (convolamine and scopoletin), flavonoids (kaempferol), and steroids (phytosterol and sitosterol) are all known to be present in the herb *Convolvulus pluricaulis*. Most likely, these phytoconstituents function as GABA-A-benzodiazepine agonists and bind to the GABA-A-benzodiazepine receptors, increasing the chloride ion flow and resulting in hyperpolarization of the postsynaptic membrane. A hypnotic effect from such hyperpolarization may lessen depression. It has been claimed that *Convolvulus pluricaulis* is effective in treating depression since it exhibits strong antidepressant properties [22]. *Shudha Vatsanabha* is an important ingredient in various formulations of Ayurveda. The chief effects have been on the central nervous system. The experimental study suggests anti-epileptic and neuroprotective effect of vatsanabha [23]. GABAergic actions along with antioxidant and neuroprotective activity [24]. *Agastya (Sesbania grandiflora)* has GABAergic actions along with antioxidant, anticonvulsive, anxiolytic, and neuroprotective activity [25]. *Ghrita* is lipoidal, it helps medications' characteristics enter the brain and be assimilated. By regulating the neurotransmitters, its antioxidant function provides neuroprotection and normalises the chemical alterations in the brain [26].

Scientific Validation of Unmada Gaja Kesari Rasa in Animal Model

Unmada Gaja Kesari was tested on the classical claims to be beneficial in Unmada and Apasmara in animal model. The Unmada Gaja Kesari rasa I (c) was evaluated for antidepressant activity w.s.r. to unpredictable stress induced depression. The study determined antidepressant activity of the drug against Fluoxetine hydrochloride, a standard antidepressant^[28]. The antipsychotics are expected to regulate GABA and NMDA receptors^[27]. The experiment study designed by *Joseph R et al.*, to evaluate multitargeted antipsychotic activity of Unmada Gaja Kesari 1 (d) determined that the formulation to be a novel single formulation exhibiting a combination of antidopaminergic, antiserotonergic, NMDA enhancing, and GABAergic activity^[29]. It can also be inferred that GABAergic activity regulates major neurotransmitters such as dopamine, serotonin, acetylcholine and noradrenaline, thus the formulation appears to have anti-epileptic activity^[29]. Unmada Gaja Kesari Rasa II (a) was studied for its antipsychotic activity by *Jyoti S, et al.*,^[30]. The study concluded that, Unmada Gaja Kesari Rasa showed antipsychotic effect after the prolonged administration. Unmada gaja kesari rasa did not show any catalepsy (adverse effect of

antipsychotic medicines). The drug was also found to be nontoxic at 2000mg/kg dose. The same formulation was also studied by *Dr. Amit P Jain*. The study determined the antiepileptic activity of Unmada Gaja Kesari Rasa II [31]. No studies have been carried out to explore the therapeutic effect of Unmada Gaja Kesari Rasa I (a), (b), Unmada Gaja Kesari Rasa II (b) and Unmada Gaja Kesari Rasa III.

Probable mode of action

By virtue of possess *Ushna Veerya* (hot in potency), *Teekshna* (sharp), *Snigdha* (unctuous) *Guna* (quality), *Tikta Rasa* (bitter in taste), and *Kaphavatahara* property (*kapha* and *vata* alleviating property) present in some of the ingredients such as *Shankhapushpi*, *Vacha*, *Gomutra*, *Brahmi*, *Datura seeds*, *Manshila*, the preparation acts on various psychiatric illness. The *ushna* and *teekshna guna* removes *tamo/ kapha avarana* thus acts as *srotoshodhana* thereby acts as anti-depressant. *Tikta rasa* itself is *Medhya* in action and hence each ingredient act as *Medhya* and help alleviate *ashta vibhrma* (8 types of instability) of mind ultimately mitigate *Unmada* and *Apasmara*. *Deepana*, *pachana*, *shothahara* property mitigates further vitiated *kapha*. All the ingredients initially act on *agni* there by correcting the gut microbiota. The preparation acts on gut brain axis and help alleviate various psychiatric disorder.

Bhavana is a unique pharmaceutical process that potentiates the drug and modifies its features. The process is carried out with a drug or combination of drugs triturated in a liquid media until it gets absorbed. Liquid media is a key element of Bhavana and its effect has been validated in a phyto pharmacognostic study. Decoction or Juice extracted from plant or animal product viz urine, milk etc are liquid media are mentioned in Ayurvedic pharmaceuticals. In Unmada Gaja Kesari Rasa, *Vacaha*, *Shankhapushpi*, *Brahmi* are commonly used in decoction and *swarasa* form as trituration *dravya*. These *dravya* may further potentiate the therapeutic efficacy by enhancing bioavailability and further absorption into the system. Bhavana help incorporate the property of liquid media into the powdered drugs to be triturated. It undergoes various physical and physico-chemical changes such as reduction in particle size, reduction in hardness, increase in weight, favours the chemical alteration [32]. In Unmada Gaja Kesari Rasa, the bioactive compounds of *Vacha*, *Shankhapushpi*, *Brahmi* get transferred to the herbo-mineral powdered ingredients thus enhances absorption, fast acting and bring about desired action quickly.

Future perspective

As the ingredients contain highly toxic substance such as *Vatsanabha*, *Kupeelu*,

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Gandhaka, Parada, it is pertinent to have toxic profile of the formulation. The previous study was able to establish LD 50 to be greater than 2000mg/kg. The study examining sub-acute, sub-chronic and chronic toxicity study is lacking.

CONCLUSION

Unmada Gaja Kesari Rasa is a herbo mineral preparation specifically indicated in *Unmada* and *Apasmara*. This claim was supported by an experimental investigation that clarified its antipsychotic and antiepileptic effects. The studies further determined its effectiveness in low dose and also proved the formulation to be superior to available antipsychotics. The combination was found to be nontoxic up to 2000mg/kg. All the varieties of Unmada Gaja Kesari can be tested for its effectiveness in *Unmada*, *Apasmara*, and other psychiatric illnesses.

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