



NEUROPROTECTIVE EFFECT OF KARMA T.NEPHRA PLUS TABLET: A SYSTEMATIC REVIEW OF AYURVEDIC POLYHERBAL COMPOSITION

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ABSTRACT

Introduction: Insomnia, anxiety, restlessness, depression are common neurological concerns today in majority of the population across the world due to increasing work stress and disturbed lifestyle. Pandemic of Covid-19 has further acted as an additional factor to these worsening cases. Modern treatment modality provides handful of options, which requires regular intake resulting in complete dependency over the time along with numerous side-effects. Hence, herbal approach for this diseased condition has been made. **Methodology:** Classical texts as well as related information from both printed and electronic media. **Observations and Results:** The combination of five herbs in this poly-herbal tablet exhibits therapeutic activities like anti-anxiety, anti-stress, sedative/hypnotic, tranquilizing effect and anti-oxidant activity thereby results in providing neuro-protective activity. **Conclusion:** Karma T. Nephra Plus Tablet is an effective poly-herbal tablet which can be used for the treatment of insomnia, anxiety, restlessness, disturbed sleep and depression and also acts as a neuro-protective herbal drug.

KEYWORDS : *Nidranash, Insomnia, T. Nephra Plus Tablet*

INTRODUCTION

Ayurvedic science believes that there are three pillars of life i.e., *Aahar* (diet), *Nidra* (Sleep) and *Brahmacharya* (celibacy) termed as *Trya-Upstambha*,^[1] which are said to be essential to maintain the health of the person. Following these basic principles of life, it helps one attaining disease-free and healthy body which helps in precieving the ultimate aim of life. It is evident that along with *Aahar* and *Brahmacharya*, *Nidra* also holds equal importance in attaining the pursuit of life and hence ancient seers have given considerable significance to *Nidra*. Passive and inactive living habits has led to various lifestyle related disorders over the past few decades. Growing idle working style, reduced physical activity, increased screen-time etc. are certain factors that has contributed to the ever-growing cases of stress, anxiety, restlessness and all these factors affect the normal sleep pattern of human body. Also, pandemic of COVID-19 has been a major conducive attribute in increasing the cases of neurological problems specifically associated with disturbed sleep, lack of sleep, anxiety, restlessness, depression etc. Insomnia is a common term used for poor sleep, difficulty in initiating or maintaining sleep. Insomnia is generally caused by the aggravation of the bodily *Vata* and *Pitta dosha*, an aggravated state of mind, loss of vital fluid or due to any injury.^[2] There are certain other factors mentioned which are responsible for *Nidranash* in classics as- fear, anxiety, anger, smoke, bloodletting, excessive physical exertion, fasting, predominance of *Satwa* and suppression of *Tamas*. Lack of proper sleep affects the day-to-day activity and also impairs the ability to function properly. Affected individuals often experiences fatigue, mood disturbances, irritability, malaise and cognitive impairment. In preview of the above mentioned conditions, Karma Ayurveda has introduced Karma T. Nephra Plus Tablet to manage the insomnia and its associated conditions. This article is planned with the view to highlight the neuroprotective effect of this polyherbal medicine which consists of 5 potent herbs.

MATERIALS AND METHODOLOGY

Drug selected for the review is KARMA T. NEPHRA PLUS Tablet manufactured by KRM AYURVEDA PRIVATE LTD., Kundli, Haryana. The resources referred for the complete review includes- The Textbook of 'Bhavaprakasha Nighantu' by

Acharya Bhavamishra, Textbook of 'Reviews on Indian Medicinal Plants' by ICMR, The Ayurvedic Pharmacopoeia of India by Government of India, Ministry of AYUSH, The Ayurvedic Formulary of India by Government of India, Ministry of AYUSH, published research articles in different journals available online, various databases and search engines.

OBSERVATIONS & RESULT

Karma T. Nephra Plus Tablet consists of a combination of following 5 Ayurvedic herbs- *Sarpagandha*, *Khurasni Ajvain*, *Jatamansi*, *Pipalimool*, *Amalaki*. The detailed description has been mentioned below in Table 1.

Table 1: Ingredients of Karma T. Nephra Plus Tablet

S.no.	Ingredient	Botanical Name	Part Used	Qty./250 mg
1.	<i>Sarpagandha</i>	<i>Rauwolfia serpentina</i>	Root	80 Part
2.	<i>Khurasni Ajvain Ghan Sattava</i>	<i>Hyoscyamus niger</i>	Seed	16 Part
3.	<i>Jatamasi</i>	<i>Nardostachys jatamansi</i>	Rhizome	8 Part
4.	<i>Pipalimoola</i>	<i>Piper longum</i>	Root	1 Part
5.	<i>Amalaki</i>	<i>Emblica officinalis</i>	Fruit	1 Part

Herbs selected for the composition of this formulation possess active constituents which acts as neuro-protective agents. Classical texts of Ayurveda has also mentioned these drugs either as single herb or in combination for the treatment of various neurological conditions like *Apasamara*, *Unmada*, *Anidra*, diseases originating due to *Vataja dosha* etc. Also, it has been observed after various pharmacological, experimental and clinical screenings that these herbs exhibits various properties which are useful as neuro-protective drugs.

After screening classical texts following biological properties of the ingredients were found as described in Table 2.

Table 2: Classical properties of ingredients of T. Nephra Plus Tablet

S.no.	Ingredient	Classical property
1.	Sarpagandha	Vatik-unmadahar, Anidranashak, Mansikvikar nashak. [4]
2.	Khurasani Ajvain Ghan Sattva	Avsadak, Swapjanak, Shamak, Nidrakar, Apasmrhar, Unmadahar, Nidrabhanganganashak, Mansik Aswasthatanashak. [5]
3.	Jatamansi	Medhajanak, Apasmarnashak, Medhya. [6]
4.	Pippalimoola	Vataroganashak [7]
5.	Āmalaki	Smritivardhak, Medhavardhak. [8]

Presence of multiple active phyto-constituents in the ingredients of T. NEPHRA- PLUS Tablet helps in possessing various desirable biological activities. Description of properties after analysis is described in Table 3.

Table 3: Biological Properties of Ingredients of T. Nephra Plus Tablet

S.no.	Ingredient	Biological Activity	Study Details
1.	Sarpagandha	a) Sedative/Hypnotic	a) The alcohol soluble fraction isolated from the root collected from Dehradun [9], Assam, Bengal and Bihar [10] (1 mg/kg, p.o.) produced sedative/hypnotic effect in guinea pig, rabbit, rat, frog and cat. The effect in cat was seen after 3-4 h of administration and it lasted for more than 24 hr.
		b) Depressant	b) Oral administration of reserpine (100 µg/kg) and Serpina tablets (total alkaloids) revealed CNS depressant effect in general behaviour of monkey and dog. Further, it was reported that 5 mg of reserpine produced equivalent degree of depression as 6 tablets of Serpina in monkey. [11]
		c) Anti-oxidant	c) The methanolic extract of the root exhibited in vitro antioxidant activity using DPPH, ABTS and FRAP scavenging assays with 0.45, 1.78 and 0.63 TEAC mg/g, respectively. [12] In another study, the aqueous and methanolic (50 and 100 per cent) extracts of the leaf at 50-250 µg/ml also showed in vitro antioxidant activity using DPPH and H2O2 radical scavenging assays. [13]
2.	Khurasani Ajvain Ghan Sattva	a) Sedative	a) Scopolamine (d-hyoscine), an important alkaloid, acts similar to atropine as competitive antagonists of peripheral and central muscarinic cholinergic receptors, [14] but it passes off more quickly. However, scopolamine has shorter effect on peripheral nervous system than atropine and is able to depress the CNS in small doses as much as 0.5 mg. [15]
3.	Jatamansi	a) Tranquilizing/Sedative	a) Treatment with the ethanolic extract of the roots at 200 mg/kg/d p.o. for 15 days in irradiated (6 Gy) mice exhibited antidepressant activity by reducing immobility time in forced swim and tail suspension tests. [16] The methanolic extract of the roots (200 mg/kg i.p.) showed CNS depressant activity in male Swiss albino mice as evidenced by decreased (22.91-61.69 %) locomotor activity of mice after drug administration (45-135 min). The depressant effect of the extract was compared with that of the standard drug diazepam (5 mg/kg i.p.).[17]
		b) Anti-stress	b) The 70 per cent ethanolic extract of the rhizomes (200 and 500 mg/kg bw p.o. for 21 days) showed adaptogenic activity in forced swimming-induced chronic fatigue syndrome in male Wistar albino rats, also reduction in anxiety levels was evidenced. This antistress effect of the extract is attributed to its antioxidant activity. [18]
4.	Pippalimoola	a) Anti-stress	a) Pre-treatment with piperlongumine (5 mg/kg p.o.) and methanolic extract of the fruit (5 mg/kg p.o. for 10 days) exhibited protection against foot shock stress triggered hyperthermia, on 11th, 15th, 17th and 20th day followed by tail suspension test on 21st day. The activity was exhibited by reducing the elevated body temperature, plasma glucose and cortisol level, ulcer index and increasing plasma insulin level. Doxycycline (50 mg/kg) also exhibited similar effects. [19]
		b) Anti-anxiety	b) Treatment with piperine at 5, 10 and 20 mg/kg i.p. exhibited dose-dependent antianxiety activity in unstressed and stressed mice as assessed by elevated plus maze test, light and dark box test and social interaction test. Piperine significantly increased brain GABA levels but did not produce any change in plasma nitrite level in unstressed mice. [20]

		c) Hypnotic	c) Pretreatment with piperine isolated at 5, 10, 25 and 50 mg/kg p.o at varying interval (0, 30, 60, 120 and 240 min) in male albino rats receiving pentobarbitone resulted in dose-dependent potentiation of phenobarbitone-induced sleeping time with peak effect at 30 min. Treatment also elevated the blood and brain pentobarbitone levels. However, treatment in chronically (100 mg/kg p.o. for 7 days) treated rats with phenobarbitone, significantly potentiated pentobarbitone sleeping time as compared to the control.[21]
		d) Bio-availability	d) The use of fruit powder and their pure component piperine protected vasicine from oxidative enzymes of liver in female rats. This provided higher concentration of unaltered vasicine in the blood. [22] Oral administration of piperine at 170mg/kg resulted in 10.8 percent maximum distribution in tissues (liver, kidney and intestine). However, the absorption rate was reported to be 96 percent. [23]
5.	Amalaki	a) Anti-oxidant	a) Oral administration of aqueous extract of the ripe fruits (2 mg/animal/d for 45 days) along with ochratoxin (50 and 100 μ g in 0.2 ml olive oil/animal/d for 45 days) showed a dose dependent amelioration of the ochratoxin-induced lipid peroxidation by increasing the contents of non-enzymatic (glutathione and total ascorbic acid) and activities of enzymatic [superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX), glutathione reductase (GR) and glutathione transferase (GST)] antioxidants. [24],[25],[26]

3. *Jatamansi (Nardostachys jatamansi)*-

4g of *Jatamansi* Churna with milk was administered thrice a day after food for a period of 1 month. After completion of treatment, it was observed that *Jatamansi* provided improvement in initiation of sleep (61.34%; $P < 0.001$), duration of sleep (48.25%; $P < 0.001$), disturbed sleep (53.08%; $P < 0.001$), and disturbance in routine works (43.85%; $P < 0.001$).^[29]

4. *Pippalimool (Piper longum)*-

Pippalimoola with Guda was given orally to the patients at a dose of 4gm/day for a period of 15 days. Out of total enrolled patients, 35% showed marked improvement, 55% patient showed moderate improvement, 10 % showed mild improvement. Significant results were observed in all the patients.^[30]

5. *Amalaki (Emblica officinalis)*-

500 mg per day of *Amla* Churna was given orally to all the patients after breakfast and dinner for 4 weeks. The study concluded that *Amla* formulation showed a significant improvement in endothelial function as well as a reduction in biomarkers of oxidative stress. Also, the results suggest that *Amla* intake may increase plasma antioxidant potential and decrease oxidative stress, which can help promote oxidative homeostasis. Reduced oxidative stress helps in improving sleep pattern and thus is beneficial for insomnia.^[31]

DISCUSSION

Lack of sleep is either due to some underlying issue or often accompanied with other symptoms such as anxiety, depression, restlessness etc. To overcome these conditions, a combination of these five herbs has been formulated. Many experimental studies conducted has reported that oxidative stress, an imbalance between the production and scavenging of ROS by the antioxidant defense system, played an important role in sleep problems. Oxidative Balance Score (OBS) also affects the sleep pattern of an individual. Studies have reported that higher the OBS values, longer is the sleep duration. Apart from prolonging the duration, greater OBS score also enhances the sleep quality.^[32] Anti-oxidant potential of herbs used in this formulation such as *Amalaki* and *Sarpagandha* are well evaluated in various experimental studies. Hence, these herbs helps in lowering the oxidative stress and provides beneficial results in sleeplessness or disturbed sleep.

Sleep is a complex process and is regulated with the help of

various neurotransmitters. Norepinephrine, 5-hydroxy tryptamine and GABA mainly controls the sleep-wake pattern. *Sarpagandha* consists of of various active phyto-constituents including mainly alkaloids such as reserpine, deserpidine, cajmaline, yohimbine etc. Reserpine is known for its sedative and tranquilizing effect. Reserpine increases GABA receptor binding activity and activates GABA-ergic cells in the basal forebrain. Reserpine also depletes 5-hydroxytryptamine, norepinephrine and dopamine from brain tissues. These neurotransmitters (norepinephrine and serotonin) promotes wakefulness and reserpine inhibits these to coordinate sleep onset and hence is effective in the treatment of insomnia, anxiety, depression etc.^[33,34]

Jatamansi is said to possess CNS depressant activity predominantly in various research works. It significantly decreases spontaneous locomotor activity and also reduces the excitability of the CNS. Studies have shown that it shortens the sleep latency and prolongs total sleeping time. All these attributes points that the herb is very helpful in reducing the hyperactivity, restlessness and induces sleep in the patients of anxiety and insomnia.^[35]

Also, presence of active constituents like piperine in *Piper longum* increases the bio-availability of the drug in the body. It enhances the absorption and yields maximum efficacy with faster action.

CONCLUSION

T. Nephra Plus Tablet by KRM Ayurveda Private Limited is an effective Ayurvedic proprietary formulation which acts as neuro-protective composition. The ingredients of this formulation are reported to possess hypnotic/sedative, anti-oxidant and anti-stress activities. It is effective in managing the conditions like Insomnia (*Anidra*), disturbed sleep, anxiety, restlessness etc.

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