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CRITICAL REVIEW FOR ASSESSMENT OF THERAPEUTIC EFFICACY OF ASHWAGANDHA IN DIFFERENT DOSES FORMS W. S. R. TO CHURNA, GRITAAND ARISHTA FORM

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ABSTRACT

Ashwagandha, Lt. Name Withania Somnifera, Solanaceae family is an annual evergreen shrub.It is used as single as well as ingredient of polyherbal formulation. It is used as dietary supplement also. **Aim:**– Assessment of therapeutic efficacy of *Ashwagandha* in different doses forms especially basic doses forms like *Ashwagandha churna*, *Ashwagandha ghrita* and *Ashwagandharishta*. **Methodology:-** Basic information about *Ashwagandha* and their forms collected from *Ayurvedic* classical books and their assessment done on the basis of Research article published related to *Ashwagandha* and *Ashwagandha kalpa*. **Result:** - *Ashwagandha* is*Kashay, tikta rasa, Ushna veerya, Laghu snigdha guna, Vatahar, Shukral* and *Vajeekarana dravya. Ashwagandha churna* has the potential to stimulated cell mediated immunity and also have good sedative property. *Ashwagandha ghrita* specially recommended in *Vatvyadhi* due toits *bruhana* and *balya effect*. It is also recommended in *Karshya, Ksheeraj phakka* in oral form. It shows effective in *basti* form to children to old age for *karshya* and osteo arthritis and *katigraha*. In Infertility in males and female it shows significant result in the form of *uttarbasti. Ashwagandharishta* exhibits significant anticonvulsant activity, significantly reduce serum cholesterol level, serum LDL and serum triglycerides. It shows diuretic, natriuretic andkaliuretic effect.

KEYWORDS: *Ashwagandha churna, Ashwagandha Ghrita, Ashwagandharishta* etc.

INTRODUCTION

Withania Somnifera belong to Solanaceae family and commonly known as *Ashwagandha*, Indian Ginseng or Winter Cherry. It is an annual evergreen shrub that grow in dry parts in sub- tropical region. Rajasthan, Punjab, Haryana, Uttar Pradesh, Gujarat, Maharashtra and Madhya Pradesh are the major *Ashwagandha* producing states of the country. The roots are stout, long tuberous, fleshy, white brown. It is generally use as a single herb or an ingredient of polyherbal or Herbo mineral formation. It is useful as medicinal herb in *Ayurveda* and use in many countries a dietary supplement. It is safe and effective for treating many diseases.[1]

It is important plant in the traditional Indian system of medicine. It is an annual evergreen shrub that grows to approximately four to five feet tall *Ashwagandha* used in more than 100 formulations in Ayurvedic formulation. It has Balya, Vrishya and Rasayan Property and suggested as substitute of *kakoli* and *kshirkakoli*. Somnifera means "Sleep inducing" in Latin indicate that it has sedative property. Its root used as an anti-inflammatory drug for swelling, scrofula, tumours, rheumatism, sedative and hypnotic in anxiety neurosis. Leaf attributes anti – inflammatory, hepatoprotective, Antibacterial properties. Fruits and seed are diuretics. The berries are used as a substitute for rennet, to coagulate milk in cheesemaking.[2]

Table 1: Shows etymology of ashwagandha.

Etymology	Explanation
Hayagandha	Root release horse's smell
Kaamroopini	It Progresses Libido
Gandhapatri	Having a smell like horse
Putrada	Be responsible for male progeny
Balada/ Balya	Encourage Strength
Marutaghni	Useful in Vata diseases

Varahakarni	Its leaves resembling pig's ear
Ashwavarohaka, Vrishya	It is Vrishya by nature

In *Charaka Sutrasthana*[4] i. e. *Aaragvadhiyaadhyaya, Ashwagandha churna* is included as *Kushthaghna*. Along with this, Ashwagandha is included in the *Mahakashayas* of the 4th chapter of *Sutrasthana*. 1) *Bruhaniya* 2) *Balya.* In *Susrutha Samhita,*[5] *Ashwagandha* is the main content of the following Gana. a) *Urdhva bhagahar* b) *Vranropana* c) *Vranautsadana* d) *Kaphashodhaghna* In 15th chapter of *Ashtang Sangraha,*[6,7] *Sutrasthana* i.e. *Mahakashayasamgraha Adhyaya, Ashwagandha* included in *Bruhaniya Gana* and *Balya Gana*. In 14th chapter of *Sutrasthana i. e. Shodhanadiganasamgraha Adhyaya, Ashwagandha* is included in *Vamanopyogi gana*.

In *Shaaramgadhara*[8] there are many medicinal preparations in which *Ashwagandha* was used as key ingredient. a) *Ashwagandhadi Churna*- It is mentioned in Madhyama Khanda*Churna Kalpanaadhyaya* as *Vajikara Kalpa*. b*) Kamdev Ghrita- Ashwagandha* is the main content of this ghrita `and is useful in *Raktapitta, Kamala, Shukrakshaya*. c) *Narayan Tail- Narayan tail* is used as *Abhyanga, Pan, Basti* in all *Vata roga*. Other preparations like *Baladi taila, Shatavari tail, Madankamdev* rasa also contents *Ashwagandha*. etc.

There are many references of *Ashwagandha* in *YogratnakarA*[9] e.g. *Trayodashanga Guggula, Yograj Guggul, Vajigandhadi kwatha, Aabhadi Churna, Mahavishagarbha Tail, Narayan Tail, Shatavaryadi yoga* etc.

Chemical constituents

The root and leaves of *Ashwagandha* contain various alkaloids viz withanolides[10] and Withaferin A[11] Among withanolides Withaferine A and Withanolide A have been reported to be dominant metabolites distributed among various tissue of this plant in varying concentrations.[12]

The main phytochemical constituents are Withanolides – which are triterpene lactones – Withaferine A, alkaloids, steroidal lactonestropins cascohygrin. Some 40 Withanolides, 12 alkaloids and numerous sitoindosides have been isolated.[13]

In addition, the root provides 18 fatty acids, beta sitasterol, polyphenols and phytosterols. The root contains several alkaloids including withanine, Withananine, pseudo- withanine, Somnine, Somniferine, Somniferinine. The leaves of Indian chemotype contain withanolides, including withaferine A.[14]

The free amino acids present in the root include aspartic acid, glycine, tyrosine, alanine, proline, tryptophan, glutamic acid and cystin.[15] The steroidal compound includes withaferine A, Withanolides G & D Sitoindosides IX & X and with asomnine. These have been reported as active marker for standardization.[16]

Prayojya anga[17] (Useful part)

Root, Leaves and *Kshar* of Withania somnifera are used in medicinalpreparations.

Dose[18]

Root Powder – 3 to 6 gm
Kshara- 1 to 3 gm

Table 2: Shows rasaguna vignyana of ashwagandha.

	Kai. Ni.[19]	**Mad. Ni.[20]**	**Dha. Ni.[21]**	**Bha. Ni.[22]**	**Ra. Ni.[23]**
Rasa	*Kashay, Tikta*	*Kashay, Tikta*	*Kashay, Tikta*	*Kashay, Tikta*	*Katu, Tikta*
Veerya	*Ushna*	*Ushna*	*Ushna*	*Ushna*	*Ushna*
Guna	*Laghu, Snigdha*	*Laghu, Snigdha*	*Laghu, Snigdha*	*Laghu, Snigdha*	*Laghu, Snigdha*
Vipaka	-	-	-	-	-

Table 3: Shows karma of ashwagandha according to various nighantu.

Nighantu	***Dosha karma***	***Dhatu karma***	***Sarvadaihika Karma***
Ra. Ni.[23]	*Vatahara*	*Shukrala*	*Vajeekarana*
Dha. Ni.[21]	*Vatkaphahar*	*Shukral*	*Vajeekarana*
Bha. Ni.[22]	*Vatakaphahar*	*Atishukrala*	*Balya, Rasayana*
Kai. Ni.[19]	*Vatkaphahar*	*Vrishya*	*Balya, Vajeekarana*
Charaka[4]			*Virechanopaga*
Sushruta[5]			*Urdhwabhaghar*

Table 4: Shows basic kalpa of ashwagandha from bhaishajya ratnavali granth.

Sr. No.	**Kalpa**	**Contents**	**Dose**	**Indication**
1	*Ashwagandha Ghrita*[24]	*Ashwagandha, Goghrit, Godugdha*		*Vatvyadhichikitsya, Vyushya, Mansavardhan*
2	*Ashwagandha Ghrita*[25]	*Ashwagandha,Goghrit,*	2 – 4 drop	*Balarogachikitsa,*

		Godugdha		*Kumaranam pushtikrud, Balavardhanam*
3	*Ashwagandha Rasayana/ Churna*[26]	*Ashwagandha Churna with Godugdha, Ghrita, Taila*		
4	*Ashwagandharishta*[27]	*Kwath Dravya – Ashwagandha, Mushali Shvet, Manjishta, Haritaki, Haridra, Daruharidra, Mulethi, Rasna, Vidarikand, Arjunchal, Nagarmotha, Nishoth, Shyam Anantmool, Annantmool shvet, Shvetchandana, lalchandan, vach, Chitrakmool, Dhatakipushpa, Madhu Prakshep – Trikatu, Trijat, Priyangu*	½ *pala*	*Murchha, Apasmar, Shosh, Unmad, Krushata, Arsha, Mandagni, Vata vyadhi*

Table 5: Shows systemic karma of ashwagandha.[28]

Sansthan	Karma	Vyadhi
Bahyasansthan	*Shothahar, Vedanasthapana*	*Granthishotha – Ushna kalka of Ashwagandha, Galagand, Granthishotha- Patralepa*
Nadisansthan	*Mastishkashamak, Nidrakara,Vatvyadhi, Balashosha, Hridaygat Vaatroga*	*Murchha, Bhrama, Anidra, Nidranash- Ashwagandha churna with mishri and ghrit, Daurbalya and Vaatvyadhi – Ashwagandha mool sidhha taila abhyanga, Ashwagandha ghrit sevan, Balashosh- Ashwagandha Churna with godugdha or ghrita or tail or ushnodaka, Ashwagandha Ghrita, Hridaygat Vaatroga – Ashwagandha churna with ushnodaka*
Pachansansthan	*Deepan, Shoolaprashaman, Krimighna,Udara roga*	*Udaravikar (Shool, Vishtambha), Krimi, Udararoga- Ashwagandha churna with gomutra*
Raktavahsansthan	*Raktabharshamak, Raktashodhak, Shothahar*	*Raktabharadhikya, Raktavikaar, Shotha*
Shwasansansthan	*Kaphaghna, Shwasahar*	*Kasa, Shwasa- Ashwagandha kshara with madhuand ghrit, Kshaya- Ashwagandha churna, pippali, sita in equal quantity with madhu and ghrit*
Prajanansansthan	*Vajikaran, Shukrala, Garbhashaya shothahar, Yonishoolahar*	*Shukradaurbalya, Pradar, Yonishula, Vandhyatva- Ashwagandha ghrit*
Satmikaran	*Balya, Bruhana, Rasayana*	*Kshaya, Shosha specially Balashosha*

In vivo studies conducted on Ashwagandha reveal that *Ashwagandha* have Adaptogenic activity, Anabolic activity, Analgesic effect, anti-inflammatory effect, anti-depressant effect, Anti-microbial activity, Anti-bacterial, Antiparkinsons, Antipyretic, Cardioprotective, Antistress activity, bradycardia and respiratory stimulant activity, Immunomodulator, neuroprotective, sedative, Thyrotropic, Hypoglycemic and hypolipidemic, Antimalerial and Nephroprotective.[29]

Preclinical studies

1. Comparative quality evaluation of Three different marketed brands of *Ashwagandha churna* (Powder) – All the parameters of three brands of *Ashwagandha churna* had approximately similar values and were compatible with the standard values mentionedin the pharmacopoeias except the values of water soluble and alcohol soluble extractive. There was considerable difference between the flow properties of the powder of all three brands. All the three brands were found to contain cadmium concentration slightly more than the prescribe value.[30]

2. Nutritional composition of dehydrated *Ashwagandha* Root Powder – Nutritional valueevaluated by AOAC (2007) standard method.[31]

Sr. No.	Component	Quantity	Sr. No.	Component	Quantity
1	Carbohydrate	49.9 gm	7	Vitamin C	5.8 mg
2	Protein	3.9 gm	8	Iron	3.3 mg
3	Fat	0.3 gm	9	Carotene	75.7micro gm

4	Energy	245 Kcal	10	Moisture	7.45%
5	Crude Fiber	32.3 gm	11	Ash	4.41 gm
6	Calcium	23 mg	12	Polyphenols	19.80g

Free radical scavenging activity (DPPH) was found to be 67.16% in Ashwagandha root powder.

3. Nutritional profiling and heavy metal analysis for Withania Somnifera based Polyherbal formulation- *Ashwagandhadi Leham Ashwagandhadi Leha* is one among the most popular avaleha preparation from Sahastrayoga.[32]

Component	**Ashwagandha Root 1**	**Ashwagandha Root 2**	**Ashwagandh avaleha**
Total Protein	0.621	1.631	0.81
Total Fat	1.138	0.328	6.7
Fiber	5%	4%	2.1 %
Carbohydrate	23.34	63.37	81.4
Chlolesterol			0
Total Sugar			52.4
Energy Value			52.4

4. Heavy metal analysis for withania somnifera

Sr. No.	**Heavy metal**	**Percentage in ppm**
1	Lead	0.19 ppm
2	Cadmium	0.15 ppm
3	Mercury	0.02 ppm
4	Arsenic	0.39pm

5. Study was planned to evaluate probable effect of *murchhana* process on ghrita preparation with reference to time and storage conditions. Result show that Ashwagandha ghrita prepared with *murchhana* process exhibited better antioxidant potential in all in vitro methods. The *murchhana* process was found to be beneficial towards quality of ghrita hence Ashwagandha ghrita may be prepared along with *murchhana* herbs and stored in a good quality glass bottle to insure improve shelf life of ghrita.[33]

6. In vivo study to evaluate Immunomodulatory activity of *Ashwagandha churna* in 5 groups (Doses 50 mg, 100mg, 200 mg, 300 mg). *Ashwagandha churna* showed significant increase in neutrophil adhesion at a dose of 300 mg kg-1 day-1 in rats which correlates with the process of margination of cells in blood vessels. The DTH response, which is a direct correlate of cell mediated immunitywas significantly increased at the dose of 200 and 300 mg Kg-1 day-1 of the *Ashwagandha churna*. During CMI responses, sensitized T Lymphocytes when challenged by the antigen are converted to lymphoblast and secrete lymphokines, attracting more scavenging cells to the site of reaction. *Ashwagandha churna* has the potential to stimulate cell mediated immunity. it may be a potential therapeutic candidate in several immunosuppressed clinical codition.[34]

7. In vivo study to evaluate Role of *Ashwagandha root churna* as first AID measures in snake venom poisoning. The present study confirms the *Vishaghna* property of *Ashwagandha* in common cobra group, at the same time *Ashwagandha* is not useful in Neurological symptoms like tremors, paralysis and convulsions. In Russel's viper venom poisoning, *Ashwagandha* is definitely useful to compensate the poisoning as well as useful in survival but requires further optimization. *Ashwagandha* does not interact with poly valent anti snake venom. Thus, *Ashwagandha* has more action cytotoxic properties of snake venom so it is useful as first aid measure in common cobrabite and Russell's Viper bite.[35]

8. Study planned to evaluate effect of *Ashwagandha ghrita* and *Ashwagandha* granules on serum lipid profile and tissue in normal rats in four groups having six animals in each. Text drug administered for fifteen consecutive days. Serum lipid profile and tissue cytoarchitecture were analyse as per standard protocol. Result was administration of both the formulation did not influence serum lipid profile and also did not alter cytoarchitecture of liver, heart, aorta and kidney. Conclusion was Ashwagandha ghrit and Ashwagandha granules do not have the potential to alter serum lipid profile.[36]

9. Study investigated whether *Ashwagandharishta* and Atasi Taila protest against maximal electroshock (MES) seizures in albino rats. MES seizures were induced for rats and seizure severity was assessed by the duration of hind limb extensor phase. Phenytoin

was used as the standard antiepileptic drug for comparison. Both flax seed oil *and Ashwagandharishta* significantly decreased convulsion phase. Pre-treatment with flax seed oil exhibited significant anticonvulsant activity by decreasing the duration of tonic extensor phase. Contrary to the expectations, pre-treatment with flax seed oil as an adjuvant to *Ashwagandharishta* failed to decrease the tonic extensor phase; however, it significantly decreased the flexion phase ($P < 0.001$) and duration of the convulsions ($P < 0.05$). Both the drugs exhibited an excellent anti-post-ictal depression effect and complete protection against mortality.[37]

10. Study evaluates the cardio protective activity of *Ashwagandharishta* T (Prepared by Traditional Method) and *Ashwagandharishta* M (Prepared by Modern Method) and marketed preparation on Isoproterenol (ISO) induced Myocardial Infraction (MI) in albino rats. Wistar albino rats of either sex were randomly divided into 06 groups comprising 06 animals in each group as normal control, ISO control, pre-treatment withInderal*10 (10 mg/kg) per os, pre-treatment with *Ashwagandharishta*-T, M and its marketed preparation at the dose of 2 ml/kg per os per day for 30 days. MI was inducedin all the groups except normal control, by administering ISO (85 mg/kg) intraperitoneally, on 29th and 30th day.Pre-treatment with Inderal*10 and all the test preparations of *Ashwagandharishta* significantly prevented the ISO-induced adverse changes in the level of serum marker enzymes as creatine kinase (CK-MB), lactate dehydrogenase (LDH), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and also improved serum lipid profile. All the test formulations pre-treated groups showed significant increase in glutathione (GSH) content and significantly reduced malonyl dialdehyde (MDA). Thus, experimental finding suggests that the cardio protective activity of *Ashwagandharishta*-T, M and its marketed preparation may be due to an augmentation of endogenous antioxidants as GSH and inhibition of lipid peroxidation of cardiac membrane.[38]

11. The antioxidant activity of *Ashwagandharishta*-T and *Ashwagandharishta*-M was found increased in concentration dependent manner in both the in vitro antioxidant activity models as super-oxide radical scavenging activity and lipid per-oxidation assay. *Ashwagandharishta*-T and *Ashwagandharishta*-M showed significant scavenging of super-oxide radical and showed IC50 91.32 and 99.39 µg/ml respectively. *Ashwagandharishta*-T and *Ashwagandharishta*-M also inhibited the ferrous sulphate induced lipid peroxidation in dose dependent manner and showed inhibitory concentration (IC50) 181.88 and 191.05 µg/ml respectively. Marketed *Ashwagandharishta* also showed a rich concentration of total phenolics and flavonoids and showed dose dependent antioxidant activity in both the models. Thus, the results obtained in this study indicate that *Ashwagandharishta*-T and *Ashwagandharishta*-M can be a promising source of natural antioxidant.[39]

12. The In vivo study designed to compare the lipid peroxidation activity and related hypolipidemic activity in *Ashwagandhrishta*-T and *Ashwagandhrishta* -M prepared by traditional and modern methods with standard Atorvastatin. Hypolipidemic activity was evaluated on cholesterol fed rats. In hypolipidemic activity *Ashwagandharishta*-T and *Ashwagandharishta*-M at the dose of 2.0ml/kg body weight orally significantly reduced serum cholesterol (47% and 46%), serum LDL (66% and 65%), and serum triglycerides (35% and 34%). The increase in serum HDL was 19% when compared to control with both the *Ashwagandharishta*T and M and reduction in atherogenic index was found 1.25 and 1.29 in *Ashwagandharishta*-T and *Ashwagandharishta*-M treated groups respectively, which strongly supports anti-atherosclerotic property of *Ashwagandharishta*.[40]

13. *Ashwagandharishta* is a polyherbal hydro – alcoholic formulation and is used as immunomodulator to promote the health and longevity by increasing defence against disease and also known for its usefulness in the treatment of Hypercholesterolemia. The amount of gallic acid in *Ashwagandharishta*- T, M and its marketed formulation was found to be 0.0281, 0.0279 and 0.0280% w/w respectively while ellagic acid was found to be 0.0191, 0.0189 and 0.0188% w/w respectfully.[41]

14. *Ashwagandharishta*-T, *Ashwagandharishta*-M prepared by traditional and modern methods respectively and marketed *Ashwagandharishta* were evaluated for antimicrobial activity against common human pathogens. It was observed that all the test preparations of *Ashwagandharishta* exhibited significant zone of inhibition against selected common human pathogens.[42]
15. A simple, precise and accurate HPTLC method has been established for the determination of quercetin and rutin in *Ashwagandharishta*–T and *Ashwagandharishta*- M prepared by traditional and modern methods respectively and also in its marketed formulation. The amount of quercetin in *Ashwagandharishta*-T, M and its marketed formulation was found to be 0.0021, 0.00192 and 0.00197% w/w respectively while rutin was found to be 0.00469, 0.00441 and 0.00464% w/w respectively.[43]

16. The objective of the in vivo study was to evaluate

the chances of reduction in cardiovascular risk factors associated with diabetic conditions. Both types of *Ashwagandharishta*-T and *Ashwagandharishta*-M, were prepared by traditional and modern methods, respectively, and evaluated for fasting blood sugar, blood glutathione levels and serum biochemical parameters in alloxan induced diabetic rats. Both the *Ashwagandharishta* preparations were able to maintain the tested parametersnear to normal level significantly.[44]

17. Molecular docking analyses have been carried out to detect any possible secondary metabolites present in *Ashwagandharishta* that could act as agonists of alpha-7 nicotinic acetylcholine receptor. According these computational findings, it has been found that two phytochemicals; anaferine and anahygrine exhibit promising agonistic activity towards the receptor. Thus, anaferine and anahygrine have high possibility toserve as alpha-7nAChR agonists which demonstrate potential drug action towards memory related disorders.[45]

18. Present in vivo study was to evaluate the diuretic effect of *Ashwagandharishta*-T and *Ashwagandharishta*-M prepared by traditional and modern methods respectively and its marketed formulation in experimental rats using Furosemide (10 mg/kg p.o) as a standard diuretic drug. Oral administration of *Ashwagandharishta*-T, *Ashwagandharishta*-M and its marketed formulation at the dose of 2.0 ml/kg over a period of 5 h showed a significant increase in urine volume as compared to control group. All the test formulations of *Ashwagandharishta* as *Ashwagandharishta*-T, *Ashwagandharishta*-M and its marketed formulation showed significant rise in sodium, potassium and chloride level in urine sample as compared to control group. The maximum diuretic effect was produced by Furosemide. Thus, both types of *Ashwagandharishta* as *Ashwagandharishta*-T and *Ashwagandharishta*-M showed significant diuretic, natriuretic and kaliuretic effects.[46]

19. Study was to analyse the effect(s) of *Ashwagandharishta* on the kidney functions of both male and female Albino rats. Chronic toxicity tests were also done. Following treatment, the rats were observed for 51 days to know the effects of *Ashwagandharishta* on kidney functions considering 3 parameters such as serum urea, creatinine and uric acid. Our results failed to exhibit a significant increase in serum urea level at low dose ($P<0.01$), medium dose ($P<0.05$) and at high dose ($P<0.001$) in male rat groups; but with female rat groups our results showed significant increase in serum urea level at three dose levels. Regarding serum creatinine level male rats and female rats showed a trend of increase in level at different dose but effects were insignificant except medium dose in male rats ($P<0.05$). Regarding serum uric acid level our results failed to show a significant increase irrespective of dose.[47]

20. An investigative analysis using reversed phase chromatography was conducted to evaluate and estimate the presence of water-soluble vitamins in seven *Asavas* and *Arishtas* namely *Drakshasava, Ashokarishta, Dashmulrishta, Khadirarishta, Lauhasava, Arjunarishta and Ashwagandharishta*. The study revealed that these preparations contained water soluble vitamins B1, B2, B3 & B6 in significant concentrations.[48]

21. In vivo study designed to study the effect of a polyherbal liquid formulation *Ashwagandharishta* on experimental gastric ulceration by Pylorus ligation ulcer model in albino wistar rats. Two different doses (2.7 ml/kg & 8.1 ml/kg) of *Ashwagandharishta* were used for investigation. Gastric mucosal protection was evaluated by measuring the ulcer index, gastric volume of secretion, total acidity and free acidity. *Ashwagandharishta* showed significant reduction in ulcer index, gastric volume, free acidity and total acidity at 2.7 ml/kg and 8.1 ml/kg compared to control group animals. Protection index was found to be 77.77% at 2.7 ml/kg and 83.33% at 8.1 ml/kg. The standard drug Omeprazole 20 mg/kg showed protection index of 86.66%. These results suggest, the active constituents present in the polyherbal formulation possess gastric ulcer healing property via multiple mechanisms.[49]

22. The present work is to know the types of biomolecules present in it by GC MS analysis. *Aswagandharishtam* was procured from standard Ayurvedic outlet and was subjected to Gas Chromatography Mass Spectrometry after due processing. The GC MS analysis of *Aswagandharishtam* has shown some promising molecules like Prostaglandin A2, Cholesterol, Piperine, Gentamicin a, d-Mannose, Eugenol, Pipradrol among others, which have activities similar to that of Aswagadharistham.[50]

23. The key objective of this study was to analyse the effect of ASG on different enzyme profile i.e.; Aspartate Aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline Phosphatase (ALP) and Lactate dehydrogenase (LDH). A total of 40 males and 40 females were randomly assigned to the four groups, namely group I (Control: water), group II (0.625 ml/kg BW of ASG), group III (5.0 ml/kg BW of ASG), and group IV (40.0 ml/kg BW of ASG) consisting of 10 males and 10 females in each group. To detect the outcome of ASG on different enzyme profile, it was administered chronically to both male and female Sprague-Dawley rats for 51 days. The results showed significant decrease of

serum AST level in ASG treated male rat groups ($p < 0.05$) than control counterpart. In females, serum AST level in mid dose (group III) was significantly higher as compared to control ($p < 0.05$). The females from mid dose group showed significant increase in serum ALT level ($p < 0.05$) whereas other groups from male and female showed no significant changes. For the enzyme Lactate dehydrogenase, only the male rat high dose showed a significant decrease ($p < 0.05$) than the corresponding control group. No statistically significant change was noted in Alkaline Phosphatase level for both the male and female rats at three different doses.[51]

Clinical studies

1. A randomized comparative clinical study to evaluate the efficacy of *Ashwagandha churna* over *Tagar Churna* in the management for 30 days of *Nidranasha* (Insomnia). Group A administered 3 gm *Tagar churna with mahishksheera* in 20 patients at 1 hr before bedtime for 30 days. Group B administered 3 gm *Ashwagandha churna with mahisha ksheera* 1 hr bedtime in 20 patients for 30 days. Athens Insomnia Scale is used to assess the result of the study. AIS Group A – 69.1% Group B – 79.09% Subjective Criteria Group A – 59.1% Group B – 74.17 %. It is clearthat Group B (*Ashwagandha Churna*) has showed more significant result than group A (*Tagar Churna*).[52]

2. A Clinical study on *Ashwagandha Ghrita* and *Ashwagandha granules* for its *Bruhana* and *Balya* effect. The study was planned to clinically evaluate AshwagandhaGhrita and Ashwagandha Granules for their *Bruhana and Balya effect*. Group A (*Ashwagandha Ghrita*) shows better response than Group B (*Ashwagandha Granules*), Group C (Placebo Group) Which clearly indicates the superiority of *Ashwagandha ghrita* as far as *bruhana* activity is concerned showed 34.97% of improvement in all the 18 cardinal symptoms whereas 23.72 % improvement was observed in group B where *Ashwagandha granules* were administered. Group C placebo treated group showed 16.99% improvement. This show that the *Ashwagandha Ghrita* is more effective than Ashwagandha granules and placebo. The drug Ashwagandha contains natural steroid that enhance the protein synthesis and lipophilic activity that allow it topenetrate the cell membrane. An increase in the capacity of internal organs too could be seen, with the increase in power of lungs probably caused by increased amount of alveolar line protein of lungs.[53]

3. Present study has been planned to evaluate the effect of *Ashwagandha ghrita* on physical growth and development of Infants, in terms of change occurred in anthropometry and milestone during the study period. The study was conducted on 40 healthy infants for a period of 12 weeks divided into two group in a dose of 0.5 ml/kg/day with milk for 4 weeks. After the completion of trial, *Ashwagandha ghrita* isfound to be beneficial in growth parameters like weight & Crown heel length. And also shows significant result on development of infants compared to control group. *Ashwagandha Ghrita* showed better effect on physical growth in terms of increment in weight, head circumference, chest circumference. Crown to heel length as well as early significant achievement of developmental milestones compared to control group. No adverse effect of the trial drug was observed during the study.[54]

4. Study was designed to evaluate the effect of *Ashwagandha Ghrita matra basti* on *Karshya* (Underweight) in children. 30 patients were allocated into two group of 15 patients each. Study group were given abhyanga with *Tila taila* and *Nadisweda* followed *by matra basti* with *Ashwagandha ghrita* along with dietary advise for 15 days. Control group given only dietary advice for 15 days. Age group 6 to 10 yrs. It was found that Matra Basti with *Ashwagandha Ghrita* showed highly significant results in subjective as well as objective parameters such as general weakness, state of hunger, activity or interest, weight in Kg, height in cm, chest circumference, mid arm circumference and B.M.I. *Aswagandha Ghrita Matra Basti* is effective in improving all the anthropometrical measurements and in reducing the associated complaints of *Karshya* and hence useful in the management of *Karshya* in children.[55]

5. 30 Patients belonging to 60 to 75 age group were recruited to evaluate the effect of *Ashwagandha ghrita matrabasti* in the dose of 60 ml for 9 days. Follow up period was fixed for 18 days. The Western Ontario and Mac Master osteo – arthritis index (Womac) was used to assess routine functions. The study showed statistically significant improvement on all three factors. *Matrabasti with Ashwagandha ghrita* curbs the pain, stiffness and discomfort in routine activity, in the patients of knee osteoarthritis belonging to geriatric age group.[56]

6. In a case study, A case of aged 30 yr male married businessman c/o Premature Ejaculation, Erectile disfunction with Infertility H/O Recurrent UTI, Investigation done Semen Analysis. Treatment was planned Uttar Basti of *Ashwagandha ghrita* (*Bhaishajya Ratnavali* 71/132) in a dose of 40 ml/ week. In this case study the sperm count prior treatment was 10 to 15 mil. / ml after 38 days of treatment Including 40 ml *Ashwagandha Ghrit uttarbasti* weekly. The significant improvement of 40 -45 mil/ml was seen in this case study.[57]

7. This study was design to evaluate the efficacy of *Ashwagandha ghrita* and *phalaghrita* in the management of *Vandhyatva* w.s.r.to Cervical Factor. In this study total total 14 patient were treated in two group. Group A (*Ashwagandha ghrita*- Intracervical *uttarbasti* 6 day for 2 cycle and *Ghrita pana* 15 ml bid for 2 months) to assess the role of ghrita in the management of *Vandhyatva*. Sim's hunter and Moghissi cervical mucus Test and Post coital test were selected for the diagnosis and forevaluation of efficacy of therapy on cervical factor. Overall effect of both the therapieson properties of cervical mucus showed that the administration of *Ashwagandha ghrita* (Group A) was more effective to increase the amount and tradability's compare to *phalaghrita*. Whereas *Phalaghrita* was more effective in comparison *to Ashwagandha ghrita* to decrease the cellularity and viscosity of cervical mucus.[58]

8. The study planned to evaluate efficacy of *Ashwagandha ghrita* on *Ksheeraj phakka*. Total 30 children were registered for the study in group A (*Ashwagandha ghrita* – 15 Childrens), Group B (Children -15) not administered *Ashwagandha ghrita*. Age group selected was below 5 yr. The result of study indicated that *Ashwagandha ghrita* along with nutritional supplement possess beneficial effect on *kheeraj phakka* due to *bruhana* effect of formulation.[59]

9. Study design to evaluate the effectiveness of *Ashwagandha ghrita* and *Dashmool taila* in the management of *Karnanad.* Total 30 patients were registered and randomlydivided into two groups. An open labelled randomized comparative clinical trial has been performed to assess the effect of *Ashwagandhadya Ghrita* and *Dashmool Taila karnapoorana* alone; both shows highly significant result in the symptoms of *Karnanada. Dashmoola Taila karnapoorana* with *Ashwagandha ghrita* is more effective in comparison to *Dashmool taila karnapoorana* alone.[60]

10. Clinical study conducted on 40 patients of Pulmonary Tuberculosis. Group A 40 patients (Only Dots Therapy) Group B – 40 Patients (*Ashwagandha ksheerpak* with DOTs therapy) Treating patients of Pulmonary tuberculosis cat-1 regimen along with *Ashwagandha ksheerpak* shows 1. Significant reduction in overall symptoms of pulmonary tuberculosis because of its Immunomodulatory and anti-inflammatory response.2. Good tolerance of anti-Koch's drug observed. 3. *Ashwagandha ksheerpak* being antioxidant and rejuvenating lead to weight gain.4. It is hepatoprotective, reduction in side effects of antitubercular drugs such as Rifampicin, Isoniazid and Pyrazinamide, hence no deranged LFT's observed.5. Sputum negativity in most of the patients (92% of trial group) observed, hence it is highly significant in treating pulmonary tuberculosis cat-1 regimen.[61]

11. This was an open-labelled single arm interventional clinical study. Fifteen diagnosed cases of *katigraha* were registered from the outpatient and inpatient department of Panchakarma and Madhur Dravya (Ashwagandha Taila) *Matrabasti* administered for 9 days. Highly significant (P< 0.0001) result was found in all the assessment parameter like Pain, Stiffness Schober's Test and functional rating Index quaternary. *Madhur Dravya (Ashwagandha Taila*) *Matrabasti* is one of the best to relieve Pain and Stiffness in *Katigraha*.[62]

12. The study includes randomized, single blind controlled comparative study with pre-test and post-test design. 408 apparently healthy subjects were screened for the features of health. 108 apparently Healthy subjects were selected by considering the inclusion criteria, and categorised into two group, (Group 1- control Group and Group 2- study Group) 54 subjects in each group. Subjects in the study group consumed 12 gm of *Ashwagandha Choorna* (powder) once daily with milk 200ml and the control group consumed milk 200 ml daily once. In the control group (n=54), the mean score overall quality of life was found to be 65.75 before intervention, after complete intervention quality of life was found to be 67.55 and at the time of follow up quality of life was found 67.55. In the study group (n=54), the mean score overall quality of life was found to be 64.38 before intervention of study, after complete intervention quality of life was found to be 71.58 and at the time of follow up quality of life was found 71.61. Subjects were improved to the higher scores among the physical, psychological domains as comparison with the environmental and social domains.[63]

DISCUSSION

After comparing three different marketed brands of *Ashwagandha churna* had approximately similar values compare with standard value except the water soluble and alcohol soluble extractive. There are different varieties of *Ashwagandha* found in India.[64] Leaves and root powder of Ashwagandha also use in food formulation. Several products are developing by researchers with Ashwagandha as food to get medicinal benefits. *Ashwagandhavaleha* is prepared from Ashwagandha root, milk and Sugar etc. which have high nutritional value. Research conducted on nutritional value of Ashwagandha root powder and *Ashwagandha avaleha* reveal that, *Ashwagandhavaleha* have rich nutritional value of carbohydrate, Total fat and energy value as compare withAshwagandha root powder. There are slight changes are visible in fibre and protein concentration in *Ashwagandha avaleha* and Ashwagandha root powder. The Ashwagandha root also contain calcium, vitamin c. Iron, Carotene and Polyphenols.

This study designed to evaluate the therapeutic efficacy of *Ashwagandha* in different doses forms like *Churna, ghrita, arishta. Ashwagandha ghrit* prepared with *murchhana* process having antioxidant potential and improve the shelf life of ghrita.

Ashwagandha churna showed significant increase in the neutrophil adhesion and delayed type hypersensitivity secrete (DTH) response lymphokines, attracting more scavenging cells to the site of reaction. It concluded that *Ashwagandha churna* has the potential to stimulate cell mediated immunity. The experimental literature indicated that withania somnifera has the potential for 1. Maintaining immune homeostasis 2 Regulating inflammation 3 Suppressing pro inflammatory cytokines 4. Organ protection (Nervous system, heart, lung, liver and kidney) and 5. Anti-stress antihypertensive and antidiabetic activity.[65]

A study designed a prospective randomized, double blind, parallel group, placebo controlled two arm exploratory study on healthy volunteer receiving the Covishield™ vaccine. The administration of Ashwagandha begin within 7 days of the first or second dose of Covishield™. The effect of Ashwagandha on the sustenance of neutralizing antibody titres up to 4 months after the second dose also evaluate in this study.[66]

Ashwagandha churna shows immunomodulatory and anti-inflammatory response due to this reveal significant reduction in overall symptoms of pulmonary tuberculosis and shows good tolerance of anti-Koch's drug observed. Administration of *Ashwagandha churna* quality of life were improved to the higher score among the physical, psychological domain as comparison with the environmental and social domain.

Ashwagandha is also useful to compensate the poisoning as well as useful in survival but re quiring further optimization. It poses Ashwagandha having *vishghna* property. *Ashwagandha churna* poses good sedative property than *tagar churna.*

This study designed to compare and analyse different doses forms of *Ashwagandha*. *Ashwagandha churna* use as a *rasayana with godugdha, ghrita, taila anupana* explained in *rasayana adhyaya of Bhaishajya ratnavali*. There are two references of *Ashwagandha ghrita in Bhaishajya ratnavali*. One in *Vatvyadhi chikitsya* and other in *Balroga chikitsya*. Contents of *Ashwagandha ghrita* are same onlydifferences found in dose calculation for children's is 2 to 4 drops.

After comparing action of *Ashwagandha ghrita* and *Ashwagandha granules* on serum lipid profile conclude that both the formulation did not influence serum lipid profile and also did not alter cytoarchitecture of liver, heart, aorta and kidney. This is good quality of *Ashwagandha ghrita*. *Ashwagandha ghrita* specially recommended in *vatvyadhi* due to its *bruhan* and *balya* effect. After comparing *Bruhan* and *Balya* effect of *Ashwagandha ghrita* and *Ashwagandha granules*. The *Ashwagandha* contain natural steroid that enhance the protein synthesis and lipophilic activity that allow it to penetrate the cell membrane.

Ashwagandha ghrita can recommended in *karshya* and *ksheeraj phakka* orally 0.5 ml/ kg/day with milk. *Ashwagandha ghrita* showed better effect on physical growth in terms of increment in weight, head circumference. Also found achievement in crown to heel length and development of milestone.

As per research conducted on *matra basti of Ashwagandha ghrita*, it can be recommended in children of above 6 yrs. for *karshya* as well as in old age group 60 to 75 yrs for knee osteoarthritis. In the form of *matra basti Ashwagandha ghrit* shows significant result. After prescribe *Ashwagandha ghrita* in the form of *matra basti* in knee osteo arthritis, it curbs the pain, stiffness and discomfort in routine activity. *Ashwagandha ghrita* shows significant result on *katigraha* also.

Ashwagandha ghrita uttarbasti can be recommended in male and female infertility. In male patient improvement seen in semen count and in female patients *Ashwagandha ghrita* shows more effective to increase the amount and tradability. *Ashwagandha ghrita* along with *dashmool taila karnapooran* shows more effective than single *dashmool taila karnapoorana*.

Ashwagandharishta mainly indicated on *Apasmara. Ashwagandharishta* exhibit significant anticonvulsant activity by decreasing the duration of tonic extensor phase. Cardio protective activity of *Ashwagandharishta* and its marketed preparation may be due to an augmentation of endogenous antioxidants as GHS and inhibition of lipid peroxidation of cardiac membrane. Self-prepared and marketed preparation of *Ashwagandharishta* showed rich concentration of total phenolics and flavonoids and showed dose dependent antioxidant activity in both the model.

Ashwagandharishta administration orally significantly reduced serum cholesterol, serum LDL and serum triglycerides. *Ashwagandharishta* showed gallic acid, ellagic acid and quercetin. *Ashwagandharishta* exhibited significant zone of inhibition against selected common human pathogen. *Ashwagandharishta* contain water soluble vitamins B1, B2, B3 & B6 in significant concentration. *Ashwagandharishta* possess gastric ulcer haling property via multiple mechanism.

Gallic acid and its derivatives have large number of applications in various field of science. They have also been implicated as anticarcinogenic, antimicrobial, antimutagenic, antiangiogenic and anti-inflammatory agent beside their use in treating critical diseases like depression, cancer, microbial infection, lipid related diseases etc.[67] Ellagic acid is naturally occurring

polyphenols found in some fruit and nuts.

Ellagic acid has been investigated extensively because of its antiproliferative action insome cancers, along with its anti – inflammatory effect.[68]

Quercetin, a polyphenol derived from plant, has wide range of biological actions including anti carcinogenic, anti-inflammatory and antiviral activities as well as attenuating lipid peroxidation, platelet aggregation and capillary permeability.[69]

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