ENTHOPHARMACOLOGICAL REVIEW OF ASHWAGANDHA ROOT EXTRACT (KSM-66®) FOR PAIN MANAGEMENT AND SLEEP

Vidhu Sethi[1], Ali Mobasheri[2], Rebecca Warren[3]

1. GSK Consumer Healthcare, Singapore, Singapore. | 2. University of Oulu, Finland; State Research Institute Centre for Innovative Medicine, Vilnius, Lithuania; World Health Organization Collaborating Center for Public Health Aspects of Musculoskeletal Health and Aging, Université de Liège, Belgium. | 3. Director of Practical Naturopathy, Sydney, Australia.

Background

- The dried root of *Withania somnifera* (L.) Dunal, commonly known as Ashwagandha, has been used in ayurvedic and indigenous medicine for ≥ 3000 years for its wide-ranging health benefits.[1]
- Both traditional and modern studies have indicated the effectiveness of Ashwagandha in pain condition and insomnia.

Objectives

- To review the traditional and scientific literature describing the safety and efficacy of Ashwagandha root extract for the management of pain and sleep.

Methods

- Literature searches were conducted on 4 December 2020 using Ayurvedic books, monographs and pharmacopoeias for traditional literature while PubMed and Embase for scientific literature on safety and efficacy of Ashwagandha root extract for the management of pain and sleep.
- There was no limitation on the publication date.
- Non–English language publications were excluded.

Results

Traditional literature have described sleep-inducing and pain-relieving properties of Ashwagandha (Figure 1)

Figure 1: Evidence from traditional literature on use of Withania somnifera (Ashwagandha) for sleep and pain management

Withania somnifera (Ashwagandha)

Sedative

Oral Dose

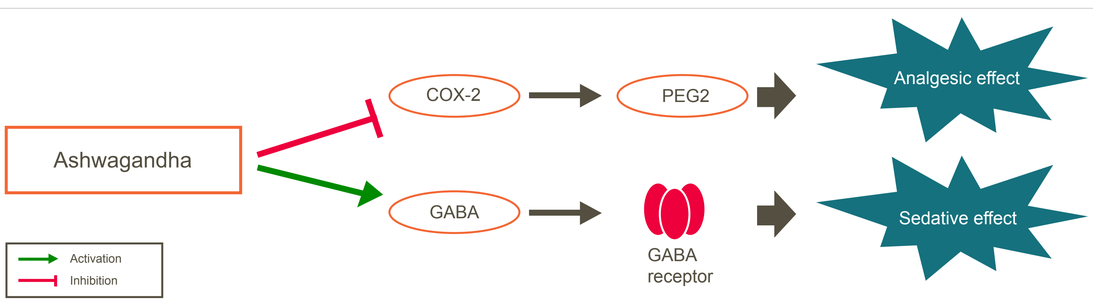
- Dried root powder; 3 - 6 g per day[1-8, 11,13]
- Dried root; 3 - 9 g per day[12]
- Dried root; 2 - 5 g per day[14]
- Dried root decoction; 3 - 8 g per day[9,10]
- Root extract (1.5% withanolides); 300-500 mg per day[1]
- Fluid extract (1:1): 3–8 ml per day[10]
- Fluid extract (1:2); 6-12 ml per day[1,11]
- Fluid extract (1:3); 6-15 ml per day[12]

Analgesic

Oral Dose

- Dried root powder; 3 - 6 g per day[11,13]
- Dried root; 3 - 9 g per day[12]
- Dried root; 2 - 5 g per day[14]
- Fluid extract (1:2); 6-12 ml per day[11]
- Fluid extract (1:3); 6-15 ml per day[12]

Ashwagandha mediates analgesic action, by inhibitingcyclo-oxygenase (COX)-2/ prostaglandins (PG)-E2 pathway[15,16] while sleep-promoting effects by promoting GABAergic action[17]



Four randomized, placebo controlled clinical trials with a total of 250 participants corroborates the ethnopharmacological use of Ashwagandha root extract (KSM-66®) for sleep (Table 1)

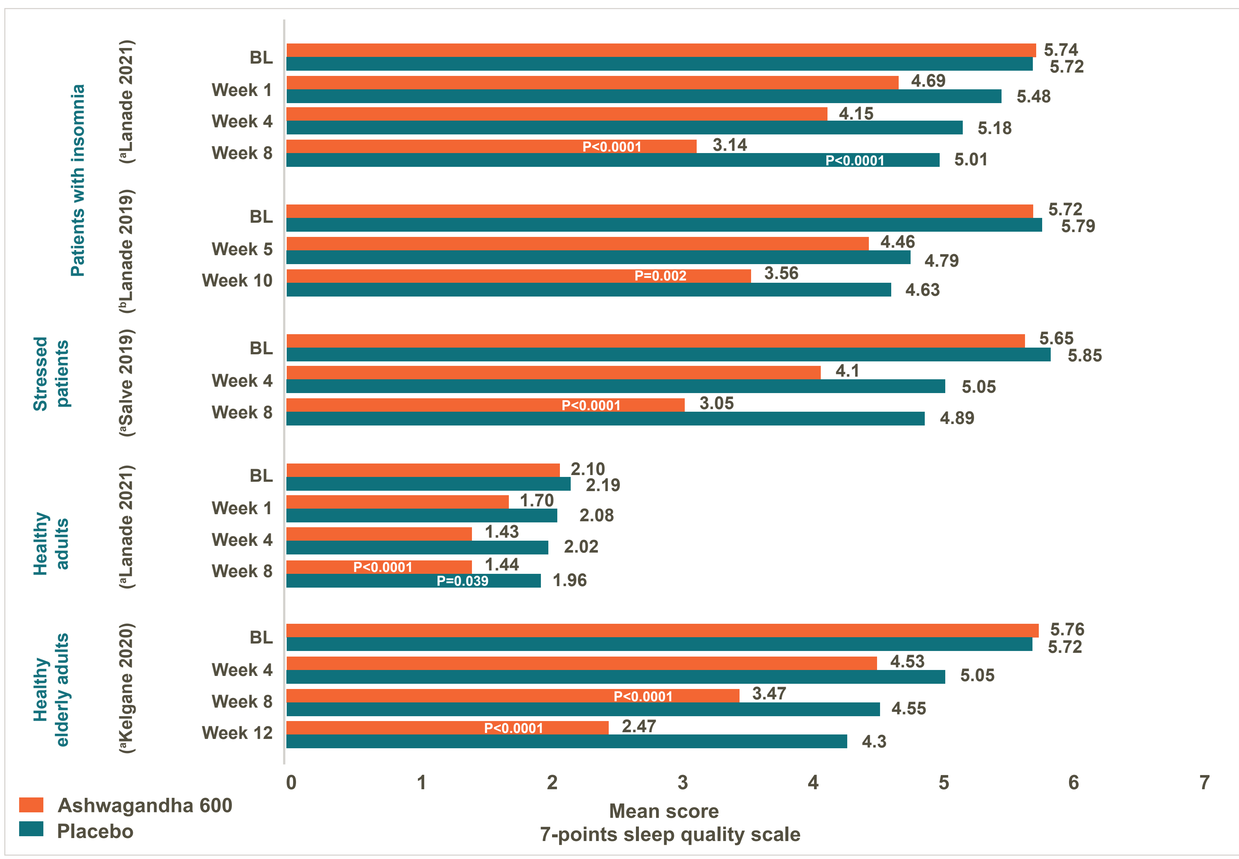
Table 1: Characteristic of included studies

Reference	Trial design	Population	Treatment arm (n) Duration of the study	Outcome of the study
Legande 2019[18]	Double-blind, Randomized, Placebo-controlled Study	60 patients with insomnia; aged between 18 and 60 years	KSM 66 capsule; 300 mg twice daily (39) vs Identical placebo (19) 10 weeks	KSM 66 capsule significantly improved sleep quality and sleep onset latency in patients with insomnia ($p < 0.0001$)
Legande 2021[19]	Double-blind, Randomized, Placebo-controlled Study	40 Healthy volunteers vs 40 patients with insomnia; aged between 18 and 60 years	KSM 66 capsule; 300 mg twice daily: Healthy (18) vs insomniac (18) subjects vs Identical placebo: Healthy (20) vs insomniac (17) subjects 8 weeks	KSM 66 capsule significantly improved sleep quality and sleep onset latency in both healthy volunteers ($p < 0.0001$) and patients with insomnia ($p < 0.002$)
Salve 2019[20]	Double-blind, Randomized, Placebo-controlled Study	60 stressed participants with Perceived Stress Scale (PSS) score >=20; aged between 18 and 60 years	KSM 66 capsule; 125 mg twice daily (19) vs KSM 66 capsule; 300 mg twice daily (20) vs Identical placebo (19) 8 weeks	KSM 66 capsule dose-dependently improved sleep quality in stressed healthy adults at 125 mg ($p < 0.05$) and 300 mg ($p < 0.001$) twice daily.
Kelgane 2020[21]	Double-blind, Randomized, Placebo-controlled Study	50 healthy elderly adults aged between 65 and 80 years	KSM 66 capsule; 300 mg twice daily (25) vs Identical placebo (25) 12 weeks	KSM 66 capsule significantly improved sleep quality ($p < 0.0001$) in healthy elderly participants

KSM 66 capsule: Ashwagandha root extract

Ashwagandha root extract (KSM-66®) exhibited significant improvement in sleep quality in healthy, insomniac, stressed and elderly subjects (Figure 2)

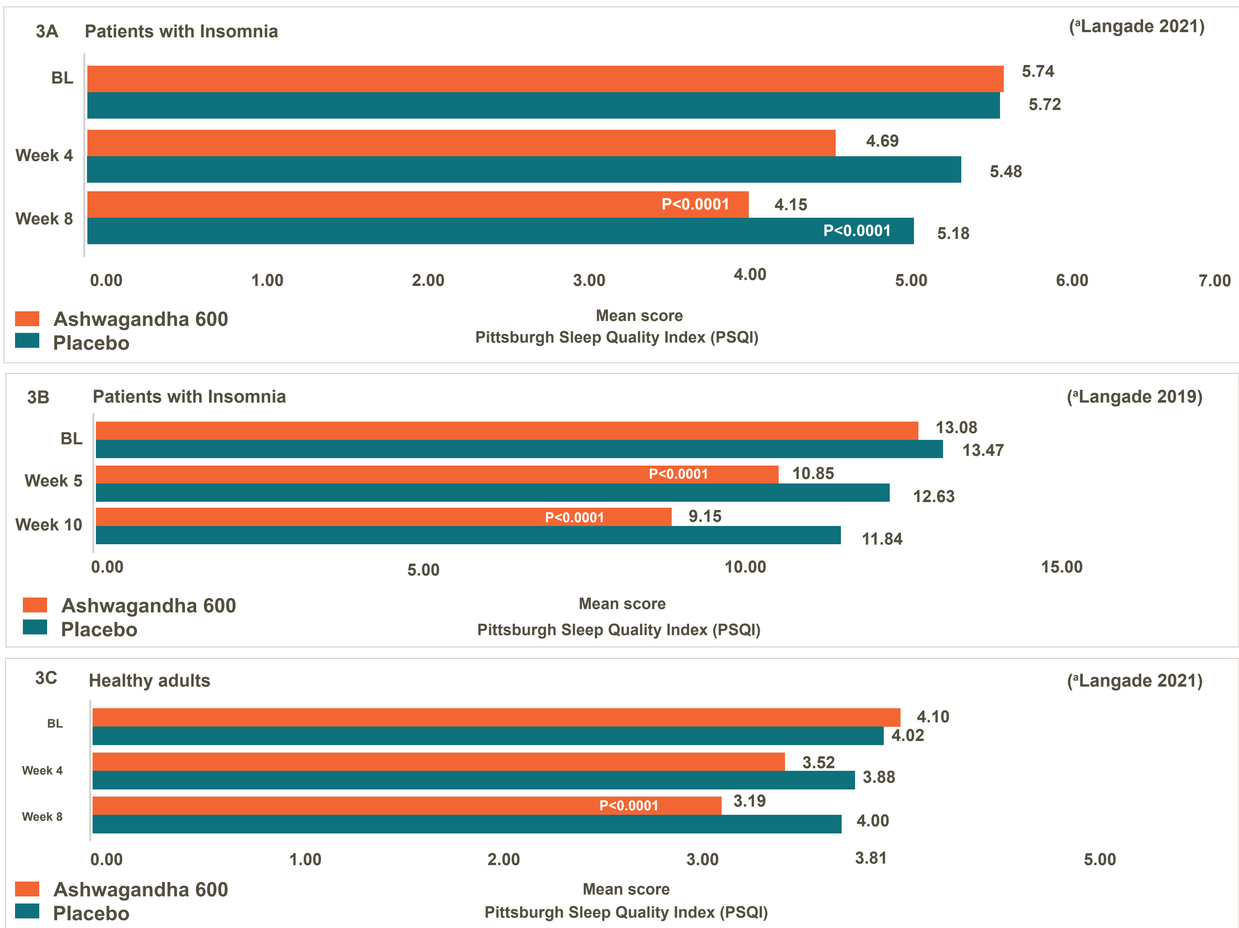
Figure 2: Efficacy of Ashwagandha root extract (KSM-66®) on 7-point sleep quality scores



[a]P-values indicate significant change from baseline to study end within a treatment arm; [b]P-value: Ashwagandha vs Placebo group

Ashwagandha root extract (KSM-66®) exhibited significant reduction in pittsburgh sleep quality index (PSQI) scores in both healthy and insomniac patients (Figure 3 [A-C])

Figure 3: Efficacy of Ashwagandha root extract (KSM-66®) on PSQI scores



[a]P-values indicate significant change from baseline to study end within a treatment arm; [b]P-value: Ashwagandha vs Placebo group

Plausible adverse reporting and safety assessment

- Ashwagandha root extract, at 300 mg twice daily, was well tolerated with no adverse events reported in all the included studies

Conclusion

- Traditional data suggest beneficial effect of Ashwagandha in the management of pain and sleep
- Scientific studies found prominent and beneficial effect of Ashwagandha root extract (KSM-66® ; 600 mg/day) in adults diagnosed with insomnia
- The use of Ashwagandha root extract is well-tolerated even up to 12 weeks of use but further studies are needed to assess whether it is safe for long-term use.

References

1. Alternative Medicine Review. Thorne Research Inc. Vol 9. No.2 2004 | 2. Bone K. Clinical applications of Ayurvedic and Chinese herbs, Phytotherapy Press. 1996. pp137-141. | 3.Health Canada Monographs. 2019 | 4. Kapoor L.D. Handbook of Ayurvedic Medicinal Plants. CRC Press, 1990. pp.337-338 | 5. Khare C.*P*. Indian Medicinal Plants an Illustrated Dictionary. Springer. 2007.pp.717-718. | 6. Upton R et al. American Herbal Pharmacopoeia and Therapeutic Compendium. American Herbal Pharmacopoeia. 2000. pp.1-25 | 7. Williamson, EM. Major Herbs of Ayurveda. Churchill Livingstone. 2002, pp.321-325 | 8. Siddha Pharmacopoeia of India (2008). Government of India Ministry of Health and Family Welfare Department of Ayush. Volume 1, pg 2-4 | 9. Van Wyk BE. Medicinal Plants of the World. Revised Edition. 2017. Pg 376 | 10. Mills S & Bone K. Principles and Practice of Phytotherapy, 2nd Ed. Churchill Livingstone. 2013. pp.949-961 pp595-602 | 11. Duke, J. Handbook of Medicinal Herbs. CRC Press. 2002. pp. 41-42 | 12. Pole S. Ayurvedic Medicine. The Principles of Traditional Practice. CRC Press. 2013. pp.133-134. | 13. Sharma PC. Database on Medicinal plants used in Ayurveda, CCRAS, Volume-3. 2001. Page 88-92. | 14. American Botanical Council (1999) | 15. Sabina E, Chandel S, Rasool MK. Evaluation of analgesic, antipyretic and ulcerogenic effect of Withaferin A. Int J Integr Biol. 2009;6(2):52-6. | 16. Ramakanth GS, et al. J Ayurveda Integr Med. 2016 Jul 1;7(3):151-7. | 17. Candelario M, et al. J Ethnopharmacol 2015 Aug 2;171:264-72. | 18. Langade D, et al. Cureus. 2019 Sep 28;11(9). | 19. Langade D, et al. J Ethnopharmacol. 2021 Jan 10;264:113276. | 20. Salve J, et al.. Cureus. 2019 Dec 25;11(12):e6466. | 21. Kelgane SB, et al. Cureus. 2020 Feb 23;12(2):e7083.

Disclosure

VS is the employee of GlaxoSmithKline (GSK) Consumer Healthcare; AM and RW were part of GSK Naturals Advisory Board

Presented at the New Zealand Pain Society 2022 Conference, Auckland

24-26 March 2022

Poster also available online at www.poster.gsk.com/XX or the QR code