A REVIEW OF RHULEAVE-K: FASTER ONSET OF NATURAL MUSCLE PAIN RELIEF

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

- Around 1.71 billion people have musculoskeletal conditions making it the leading contributor to disability worldwide.[1]
- Despite the need for a rapid onset, there is an increasing demand for naturopathic medications that deliver efficacy.

Objectives

- To review the clinical efficacy of Rhuleave-K (turmeric extract + boswellia gum extract + sesame oil), curcumin and boswellia in relieving acute muscle pain.

Methods

- A literature search was conducted using Embase and Google Scholar on the efficacy of Rhuleave-K, and monotherapy of curcumin (≤280 mg/day) and boswellia (≤100 mg/day) for the relief of muscle soreness and pain, since inception to October 2021.

Results

- A total of five randomized, controlled studies (RCTs) were identified for muscle pain indication (**Table 1**).

Table 1: Pain Relief Efficacy with Rhuleave-K from the Clinical Trials

Trial Design	Treatment Arms (n)	Study Population (N)	Study Duration	Interpretation
Rhuleave-K (Curcumin + Boswellic Acid + Sesame Oil)				
Randomized, double-blind, placebo-controlled, multicenter study [2]	Rhuleave-K 1000 mg (116) *Versus* PLA (116)	Healthy participants with acute musculoskeletal pain (N=232)	1 day (6 hours)	Rhuleave-K has shown significant pain improvement compared to placebo (PLA).
Randomized, controlled, open-label study [3]	Rhuleave-K 1000 mg/ day (44) *Versus* APAP 1000 mg/day (44)	Adult healthy subjects with acute musculoskeletal pain (N=88)	7 days	Rhuleave-K resulted in significant pain relief, which is comparable to APAP.
Curcumin Monotherapy				
Randomized, single-blind, parallel design study [4]	CUR 180 mg/day ingested for 7 days before exercise (8) *Versus* CUR 180 mg/day ingested for 4 days after exercise (8) *Versus* PLA (8)	Healthy young men with exercise-induced muscle soreness (N=24)	4-7 days	CUR ingestion after exercise has shown beneficial effect in attenuating the muscle soreness.
Randomized, double blind crossover study [5]	**Exp. 1**: (10) CUR 180 mg/day ingested for 7 days before exercise or PLA; **Exp. 2**: (10) CUR 180 mg/day ingested for 7 days after exercise or PLA	Healthy men with exercise-induced muscle damage and inflammation (N=20)	7 days	CUR improved muscle soreness, muscle strength, ROM and CK activity.
Double-blind randomized-controlled crossover trial [6]	CUR 150 mg/day (10) *Versus* PLA	Healthy young men with delayed onset muscle soreness (DOMS) induced by eccentric exercise (N=10)	1 day	CUR has shown anti-inflammatory and analgesic effects.

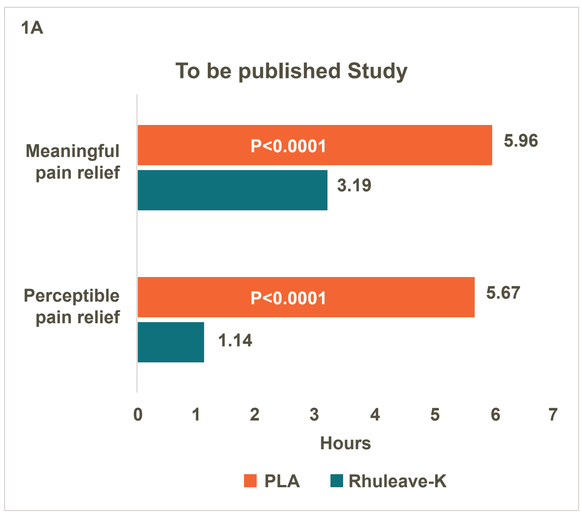
ALT: Alanine transaminase; **AST**: Aspartate transaminase; **CK**: Creatinine kinase; **CUR**: Curcumin; **MPQ**: McGill Pain Questionnaire; **PLA**: Placebo; **MVC**: Maximal voluntary contraction; **ROM**: Range of motion; **SPID6**: Sum of pain intensity difference over 6 hours; **VAS**: Visual analogue scale; **TOTPAR6**: Total pain relief over 6 hours;

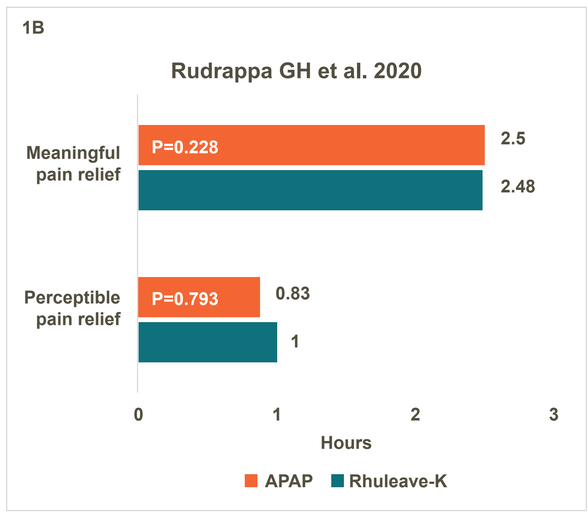
Note: No clinical study found for boswellia evaluated in muscle pain.

Efficacy

- *Onset of Analgesia:*
  - » Rhuleave-K has shown the perceptible pain relief in 99% subjects at 1.14 h, where as placebo (PLA) in 10% subjects at 5.67 h, and the meaningful pain relief in 96% subjects at 3.19 h, while PLA in 1.7% subjects at 5.96 h (**Figure 1A**). [2]
  - » Both Rhuleave-K and APAP were equally effective in the pain reduction and there was no significant difference between the groups (**Figure 1B**). [3]

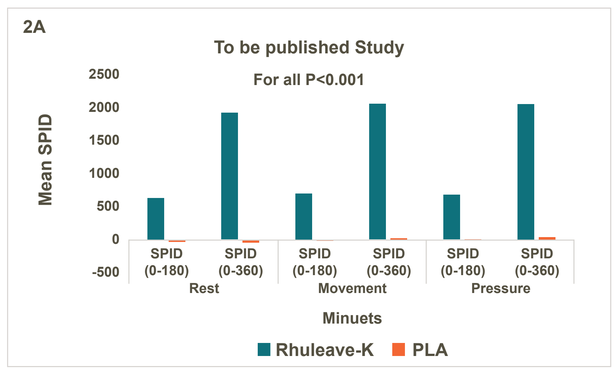
Figure 1: Onset of perceptible pain relief and meaningful pain relief

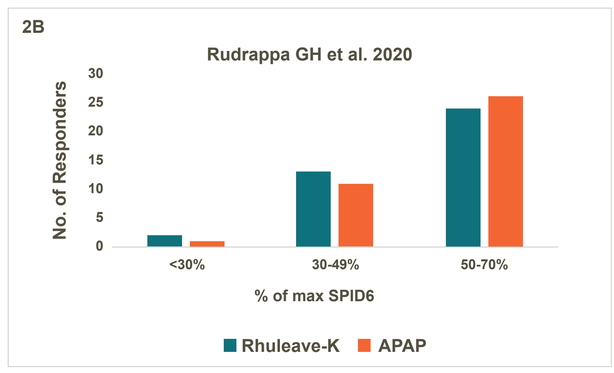




- *Sum of Pain Intensity Difference over 6 hours (SPID6) on Numeric Rating Scale (0-10):*
  - » A significant difference was observed for SPID6 between Rhuleave-K and PLA for the pain relief at rest, movement and pressure (P<0.001, **Figure 2A**). [2]
  - » The Rhuleave-K has shown significant pain reduction with 73% positive responders (≥30% Max SPID6) and comparable to the APAP with 80% positive responders **Figure 2B**). [3]

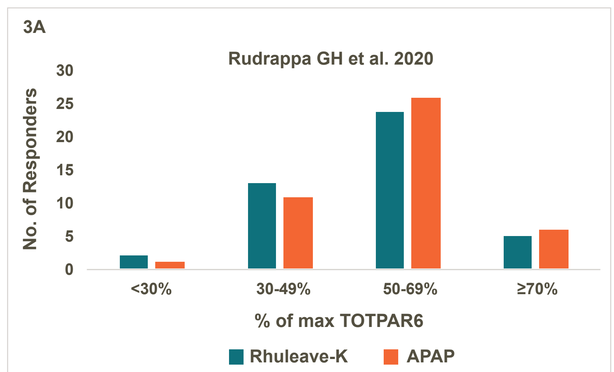
Figure 2. Time-weighted SPID and percentage of maximum SPID responders over 6 h

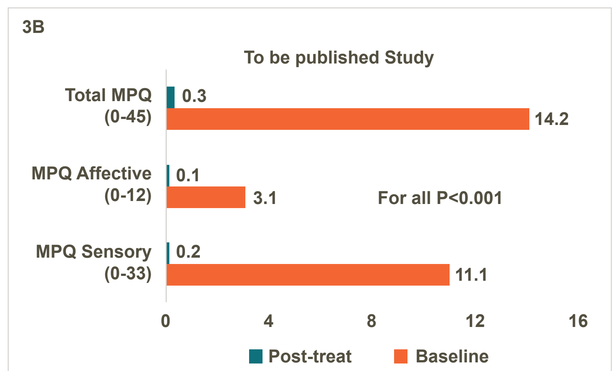




- *Total Pain Relief over 6 hours (TOTPAR6) on Pain Relief Scale (0-4):*
  - » Rhuleave-K has shown significant improvement in TOTPAR6 scores for pain at rest, movement and pressure compared to PLA (P<0.0001). [2]
  - » Around 66% of subjects in the Rhuleave-K group and 73% in the APAP group reported positive responses in pain relief (≥50% max TOTPAR) (**Figure 3A**). [3]
- *McGill Pain Questionnaire (MPQ):*
  - » A statistically significant reduction was observed in MPQ scores for total, sensory and affective domains in the Rhuleave-K group, but not in the PLA group (**Figure 3B**). [2]
  - » The total MPQ score showed significant reduction in pain with both Rhuleave-K and APAP groups and statistically equal (P=0.468). [3]

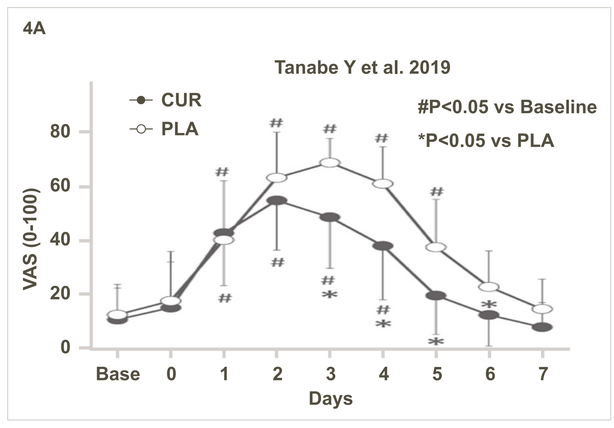
Figure 3. Percentage of maximum TOTPAR responders over 6 h and MPQ scores

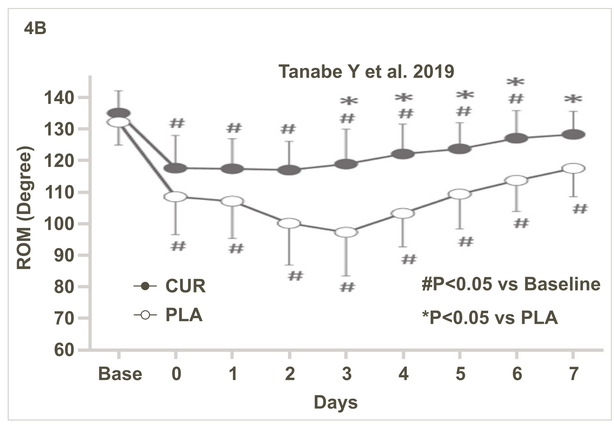




- *Muscle Damage Markers:*
  - » CUR ingested after exercise has shown beneficial effects in attenuating the muscle soreness (**Figure 4A**) and improved CK activity, range of motion (ROM) of the elbow joint (**Figure 4B**), and MVC torque of the elbow flexors when compared to PLA. [4-6]

Figure 4. Muscle soreness (VAS scores) and ROM of elbow joint (degrees)





Safety

- No adverse event reported in both the studies of Rhuleave-K [2, 3] and further long-term studies will be needed to evaluate the safety in humans.

Conclusion

- The clinical data for Rhuleave-K suggests potential analgesic and anti-inflammatory action in muscle pain with faster onset of action.
- Curcumin ingestion after exercise may attenuate muscle damage and helps in faster recovery.
- However, due to limited data availability in the literature, more studies will be needed in the future.

References

1. WHO Factsheet. (https://www.who.int/news-room/fact-sheets/detail/musculoskeletal-conditions). | 2. Rudrappa GH, et al. *To be published study (CTRI/2020/06/025601)*. | 3. Rudrappa GH, *et al. Medicine (Baltimore)*. 2020;99(28):e20373. | 4. Tanabe Y, et al. *J Nutr Sci Vitaminol (Tokyo)*. 2019;65(1):82-89. | 5. Tanabe Y, et al. *Scand J Med Sci Sports*. 2019 Apr;29(4):524-534. | 6. Nakhostin-Roohi B, et al. *Ann Appl Sport Sci*. 2016;4(2):25-31.

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