CURCUMIN AND BOSWELLIA FOR OSTEOARTHRITIS PAIN MANAGEMENT: A LITERATURE REVIEW OF C3 COMPLEX® AND APRESFLEX®

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Background

- There is a need of safe and effective pain management for osteoarthritis (OA), as the number of cases is likely to rise with the increasing elderly population[1]
  - » In Australia, the number of individuals affected is expected to grow by 30% between 2015 and 2030[2]
- *Boswellia serrata and Curcuma longa* formulated extract in combination might provide an effective and safe option in the management of OA pain[3,4]

Objectives

- To review literature describing the efficacy, safety, and bioavailability of a Boswellia extract selectively enriched with boswellic acid and Boswellia oil (ApresFlex® or Aflapin®) and curcumin with Bioperine® (C3 Complex®) for OA pain management.

Methods

- Searches were conducted on 4 December 2020 for
  - » Safety and use of curcumin and boswellic acid in OA pain using Ayurvedic books, monographs and pharmacopoeias
  - » Safety and efficacy of boswellic acid monotherapy and curcumin with piperine in OA pain using PubMed and Embase
  - » Bioavailability of boswellic acid and curcumin using PubMed and Embase
- There was no limitation on the publication date
- Non–English language publications were excluded

Results

Five Pharmacopoeias and Compendia were identified that described about the use of curcumin and boswellic acid in pain and inflammation associated with arthritis (Table 1)

Table 1. Characteristics of curcumin and boswellic acid

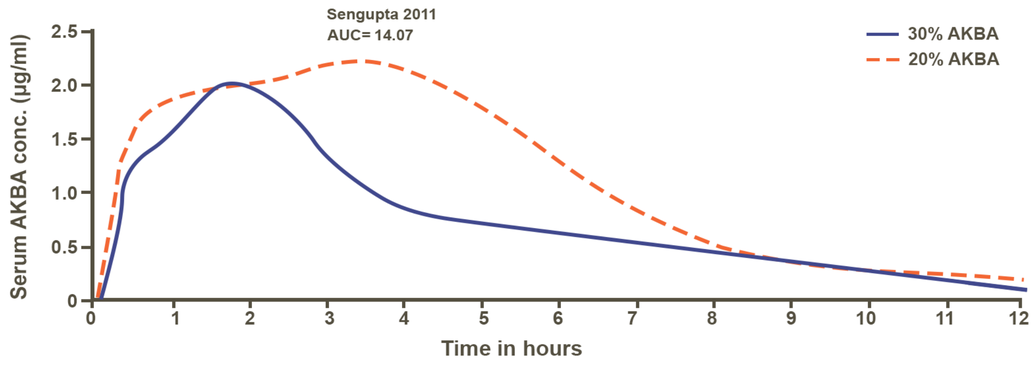
Ingredients	Listed Name and Description	Key Activities and Therapeutic Uses
Curcumin	• Haridra [5] • *Curcuma longa* L [5,6] • Turmeric [5,6] • Indian saffron [6] • Yellow ginger [6]	• Inflammation [5] • Pain [5,6]
Boswellic Acid	• Shallaki Niryas [5] • *Boswellia serrata* R [6] • Gummi boswellii [7]	• Pain and inflammation associated with arthritis [5,6,7]

Five scientific studies were identified and included in this literature review:

- 2 bioavailability studies for boswellic acid and curcumin + piperine formulation respectively were identified[8,9] (**Figure 1 & 2**)
- 3 randomized clinical trials demonstrating safety and efficacy of boswellic acid monotherapies[10,11] and curcumin with piperine[12] in patients with OA pain (**Table 2**)

Bioavailability of 20% AKBA-enriched boswellic acid formulation was 51.8% greater compared with a 30% AKBA boswellic acid formulation[8]

Figure 1: Comparative bioavailability of AKBA 20% and 30% in Sprague–Dawley rats



AKBA, 3-O-acetyl-11-keto-betaboswellic acid; **AUC**, Area under curve

- 20% AKBA standardized extract (Aflapin) provided better improvement in WOMAC pain scores compared to 30% AKBA standardized extract that can be attributed to its better bioavailability [8,11]

The relative bioavailability of curcumin increased by 2000% with concomitant piperine[9]

Figure 2: Comparative bioavailability of curcumin and curcumin + piperine in healthy human volunteers

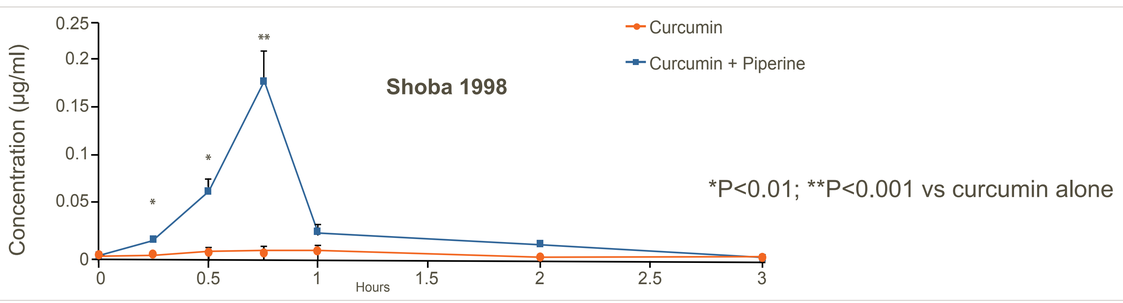


Table 2: Characteristic of included randomized controlled trials

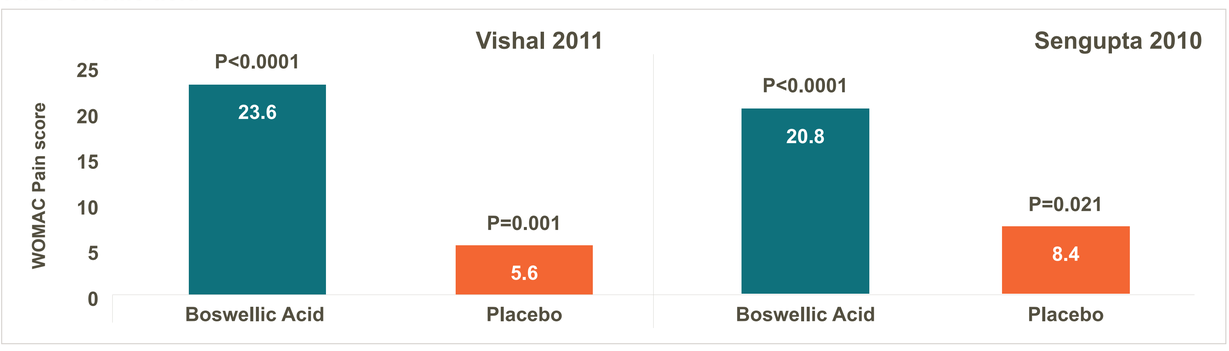
Trial Design (N)	Population	Treatment Arms (n)	Duration of study	Change in WOMAC Physical Function	Change in WOMAC Stiffness
Boswellic acid monotherapy					
Randomized, double blind, placebo controlled trial[10]	Patients diagnosed with degenerative hypertrop hic OA	Boswellic acid (20% AKBA) 50 mg twice daily (30) vs PBO (30)	30 days	• Boswellic acid: −18.6 (*P*<0.0001) • PBO: −3.8 (*P*=0.0029)	• Boswellic acid: −18.8 (*P*<0.0001) • PBO: −3.4 (*P*=0.2024)
Randomized, double blind, placebo controlled trial[11]	Patients diagnosed with medial tibiofemoral OA	Boswellic acid (20% AKBA) 100 mg/day (19) OR boswellic acid (30% AKBA) 100 mg/day (19) vs PBO (19)	90 days	• Boswellic acid (20% AKBA): −25.8 (*P*<0.0001) • Boswellic acid (30% AKBA): −17.9 (*P*<0.0001) • PBO: −10 (*P*=0.0025)	• Boswellic acid (20% AKBA): −27.7 (*P*<0.0001) • Boswellic acid (30% AKBA): −22.4 • (*P*=0.0001 PBO: −9.9 (*P*=0.0059)
Curcumin + piperine					
Randomized, double blind, placebo controlled trial[12]	Patients diagnosed with unilateral or bilateral knee OA	Curcumin + Piperine 1500 mg/day (19) vs PBO (21)	6 weeks	• Curcumin + Piperine: −13.1 (*P*<0.001) • PBO: −2.0 (*P*=0.227)	• Curcumin + Piperine: −0.90 (*P*=0.043) • PBO: −0.94 (*P*=0.009)

AKBA, 3-O-acetyl-11-keto-betaboswellic acid; **NS**, not significant; **OA**, osteoarthritis; **PBO**, placebo; **WOMAC**, Western Ontario and McMaster Universities Osteoarthritis index.

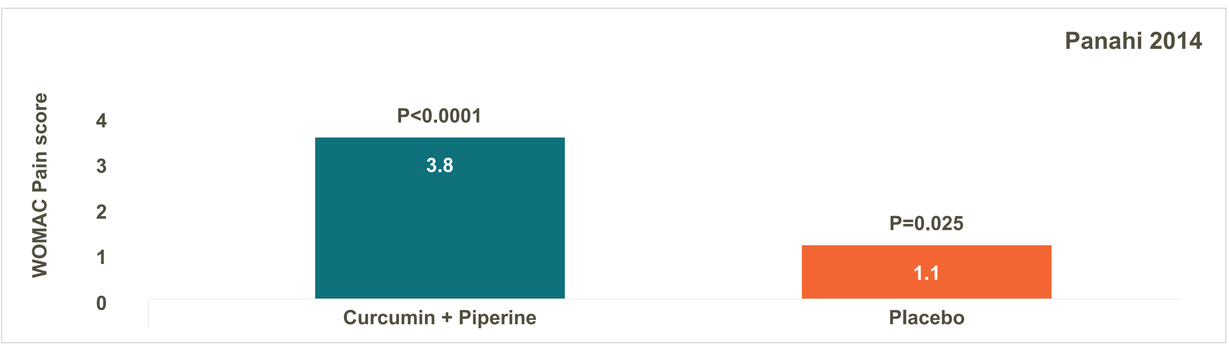
Boswellic acid monotherapies, curcumin + piperine showed significant improvement in WOMAC pain score in patents suffering from OA[10-12]

Figure 3: Efficacy of (A) Boswellic acid and (B) Curcumin on WOMAC pain score in patients with OA

A. Boswellic acid



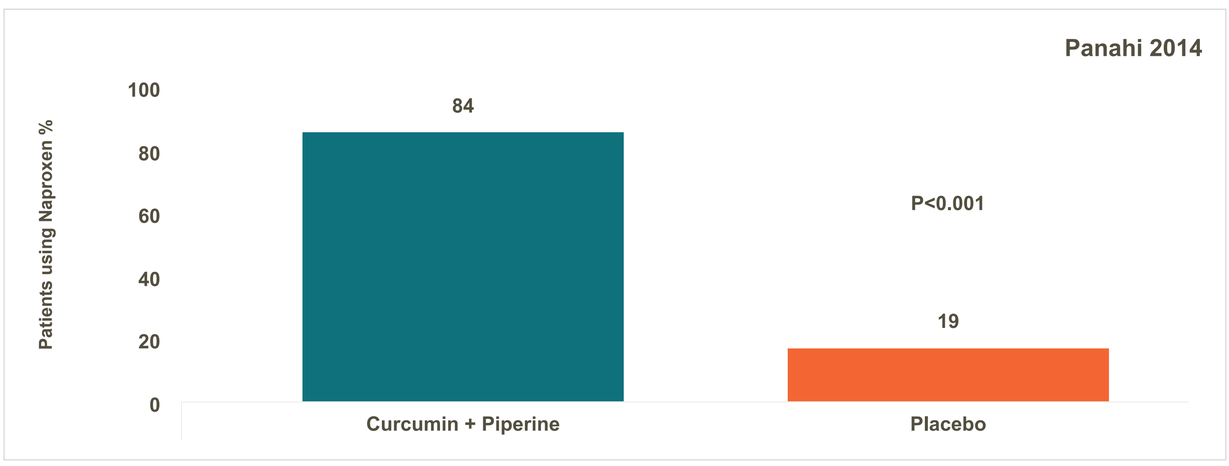
B. Curcumin



P-values indicate significant change from baseline to study end within a treatment arm.
NS, not significant; **WOMAC,** Western Ontario and McMaster Universities Osteoarthritis index.

84% of OA patients in the curcumin+piperine group showed significant reduction in the use of naproxen (rescue medication)[12]

Figure 4: Percentage of OA patients reporting reduction in the use of Naproxen (rescue medication) at the end of the study



P-value: Curcumin + piperine vs placebo group

Plausible adverse reporting and safety Assessment

- Overall, adverse events (AEs) were few and generally minor with no major events reported in the reviewed studies[10,11,12].
- Pharmacopoeias/Monographs have provided few adverse reactions and special warning associated with curcumin and boswellic acid (**Table 3**)

Table 3. Safety information on curcumin and boswellic Acid in pharmacopoeias/monographs

Ingredients	Adverse reactions	Special warnings and precautions
Curcumin	Allergic dermatitis [7] Dry mouth [13,14] Flatulence [13,14] Gastric irritation [13,14]	• Children and adolescents under 18 years of age [13,14] • During pregnancy and lactation [6,13,14] • Individuals with obstruction of the bile duct, cholangitis, liver disease, gallstones, and any other biliary diseases [6,13,14] • Individuals on anti-platelet medication or blood thinners [6]
Boswellic Acid	Minor gastrointestinal side effects[7]	• Not available

Conclusion

- Curcumin+piperine and boswellic acid monotherapy products may be considered effective natural treatment options for OA pain management
- In the randomized, controlled clinical trials included in this literature review: Curcumin+piperine and boswellic acid monotherapies improved WOMAC pain scores from baseline to end of study and improved several pain measure scores versus placebo in patients with OA.
- Piperine enhanced the serum concentration, extent of absorption and bioavailability of curcumin that might be the reason behind its improved efficacy in patients with OA pain
- No major AEs were reported with either curcumin+piperine or boswellic acid

References

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Disclosure

MG has no relevant disclosures to report; KS & VS are employees of GlaxoSmithKline Consumer Healthcare.

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