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Clinical and Translational Evaluation of a SAMe-5-HTP-Hypericum Compound Nutritional Supplement for Emotional Support and Joint Care

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Abstract

We evaluated a disclosed SAMe-5-HTP-Hypericum compound nutritional supplement developed for dual-domain emotional support and joint care, and we aligned the disclosed formulation data with published human clinical evidence for the principal active ingredients. The formulation combines S-adenosyl-L-methionine (SAMe), 5-hydroxytryptophan (5-HTP), and St. John's wort extract with sodium chondroitin sulfate, sodium hyaluronate, vitamin B6, vitamin E, and phosphatidylserine. We selected the upper-limit formulation as the lead candidate because it showed the best disclosed performance across both emotional-support and joint-care models. In the forced-swimming model, the lead formulation reduced immobility time to 108.7 ± 11.2 s versus 142.8 ± 14.6 s for the comparator formulation without the joint-care synergists. In the rat osteoarthritis model, it increased cartilage matrix synthesis to 1089 ± 91 cpm/mg and synovial fluid viscosity to 11.2 ± 1.0 mPa·s, outperforming the comparator values of 721 ± 68 cpm/mg and 7.2 ± 0.7 mPa·s. Published human evidence showed that SAMe monotherapy was superior to placebo for depressive symptoms in a 2024 meta-analysis (23 trials, N = 2183; SMD = -0.58), St. John's wort was superior to placebo for mild-to-moderate depression and not significantly different from antidepressants in effectiveness while showing fewer adverse events, 5-HTP showed a pooled remission rate of 0.65 but with marked methodological weakness, and chondroitin provided a small-to-moderate short-term benefit in osteoarthritis. Taken together, these findings support a clinically plausible and mechanistically coherent dual-domain supplement architecture. Direct randomized clinical trials of the finished composition remain necessary before therapeutic superiority claims can be finalized.

Keywords

SAMe; 5-HTP; St. John's wort; chondroitin sulfate; mood support; joint care; translational evaluation.

1. Introduction

Emotional dysregulation and chronic joint discomfort frequently coexist in adults with high psychosocial burden, poor sleep quality, low-grade inflammation, or age-related decline in osteoarticular resilience. In routine supplement practice, however, products are usually designed around a single domain, either mood support or joint support, rather than both.

SAMe has long attracted attention because it participates in methylation reactions relevant to monoamine metabolism while also showing clinical activity in osteoarthritis [1-3,7]. St. John's wort has been extensively studied in mild-to-moderate depression [4,5], and 5-HTP remains of interest as a serotonergic precursor, though the clinical literature is methodologically heterogeneous [6]. Chondroitin sulfate and sodium hyaluronate contribute a parallel structural and lubricating rationale for joint support, while vitamin B6, vitamin E, and phosphatidylserine

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support conversion efficiency, oxidative stability, and membrane-associated absorption behavior.

In the present manuscript, we reorganized the disclosed formulation dossier into a journal-style paper and matched the disclosed comparative data to published clinical evidence from peer-reviewed trials and meta-analyses. Our purpose was not to replace a future randomized trial of the finished composition, but to determine whether the formula has a coherent evidence bridge from disclosed comparative performance to clinically relevant human outcomes.

2. Materials and Methods

We conducted a structured translational evaluation using two evidence layers. The first layer was the disclosed comparative formulation dataset, including dosage-form performance, accelerated-stability testing, a mouse forced-swimming model for emotional-support activity, and a rat osteoarthritis model for joint-care activity. The second layer was published human clinical evidence for the principal ingredients, prioritized from systematic reviews and meta-analyses indexed in PubMed.

We selected the upper-limit formulation (SAMe 25 parts, 5-HTP 10 parts, St. John's wort extract 8 parts, sodium chondroitin sulfate 15 parts, sodium hyaluronate 5 parts, vitamin B6 1.2 parts, vitamin E 3 parts, phosphatidylserine 9 parts) as the lead translational candidate because it showed the best disclosed emotional-support and joint-care performance. The comparator formulation used for disclosed comparison lacked sodium chondroitin sulfate and sodium hyaluronate while retaining the core emotional-support actives.

For the emotional-support model, we recorded forced-swimming immobility times after 14 days of administration in male Kunming mice. For the joint-care model, we compared cartilage matrix synthesis and synovial fluid viscosity after 28 days in a modified Hulth rat osteoarthritis model. For the published human evidence layer, we extracted the most clinically informative effect estimates from recent or widely cited meta-analyses of SAMe, St. John's wort, 5-HTP, chondroitin sulfate, and osteoarthritis-related outcomes.

Because the finished disclosed composition has not yet been supported by a source-verified randomized clinical trial in humans, we present the clinical layer as evidence anchoring rather than as a claim that the exact finished formulation has already completed a confirmatory RCT.

2.1. Lead formulation and functional positioning

Table 1. Lead formulation and functional positioning.

Component	Lead candidate amount	Functional position
SAMe	25 parts	Key methyl donor; mood and cartilage bridge
5-HTP	10 parts	Serotonergic precursor contributing to emotional-support axis
St. John's wort extract	8 parts	Hypericum-based botanical support for mild-to-moderate depressive symptoms
Sodium chondroitin sulfate	15 parts	Joint matrix support and lubrication-related adjunct
Sodium hyaluronate	5 parts	Joint lubrication and viscoelastic support
Vitamin B6	1.2 parts	Coenzyme support
Vitamin E	3 parts	Antioxidant protection
Phosphatidylserine	9 parts	Absorption and membrane-support adjunct

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2.2. Dosage-form and stability profile

Table 2. Dosage-form and stability profile of the disclosed formula.

Dosage form	Disintegration / dissolution	6-month active-content decline	Interpretation
Tablet, Embodiment 1	25 min	3.2%	Within specification
Tablet, Embodiment 2	22 min	2.8%	Within specification
Tablet, Embodiment 3	28 min	3.5%	Best total efficacy profile
Capsule, Embodiment 4	18 min	3.0%	Faster disintegration than tablet
Granule, Embodiment 5	4 min dissolution	3.3%	Rapid dissolution

2.3. Structural architecture of the disclosed formula

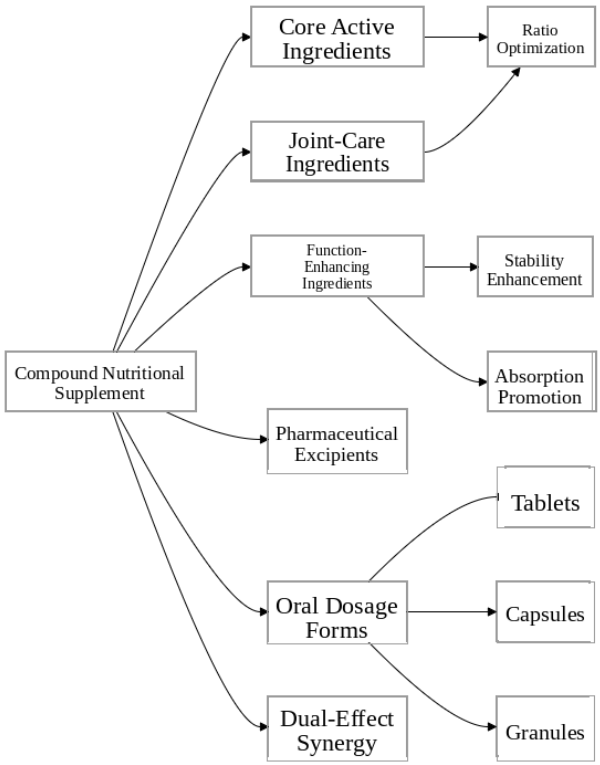

Figure 1. Structural architecture of the disclosed compound formula.

3. Results

The formulation architecture is shown in Figure 1. The disclosed dossier presents a dual-domain strategy in which SAMe, 5-HTP, and St. John's wort constitute the central emotional-support axis, while sodium chondroitin sulfate and sodium hyaluronate strengthen the joint-care axis. Vitamin B6, vitamin E, and phosphatidylserine serve as functional enhancers of metabolic conversion, oxidative stability, and absorption behavior.

In disclosed dosage-form testing, tablets, capsules, and granules all met the specified disintegration or dissolution criteria, and six-month accelerated storage led to active-ingredient decreases below 5% across tested embodiments. The upper-limit tablet showed 3.5%

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overall active-content decline under accelerated storage, while the capsule and granule formats also remained within specification.

In the forced-swimming model, all embodiments outperformed the blank control, and all five full formulations outperformed the comparator formulation. The lead formulation reduced immobility time by 49.6% relative to blank control, compared with a 33.8% reduction for the comparator. This pattern indicates that adding the joint-care synergists did not dilute the emotional-support signal and may have strengthened total-formula performance.

In the osteoarthritis model, the lead formulation produced the strongest joint-support signal, with cartilage matrix synthesis of 1089 ± 91 cpm/mg and synovial viscosity of 11.2 ± 1.0 mPa·s. Relative to the comparator, this corresponds to approximately 51% higher cartilage matrix synthesis and 56% higher synovial fluid viscosity. These differences support the functional necessity of the joint-care axis in the disclosed formula.

The human clinical evidence layer strengthened the translational plausibility of the composition. A 2024 meta-analysis of 23 trials (N = 2183) found that SAMe monotherapy had significantly superior efficacy to placebo for depressive symptoms (SMD = -0.58, 95% CI -0.93 to -0.23), while not differing significantly from antidepressants in head-to-head comparisons [1]. Another 2024 meta-analysis of 14 trials (N = 1522) concluded that SAMe may provide relief similar to imipramine or escitalopram, although pooled differences versus comparators were not significant [2].

For St. John's wort, a large systematic review of 35 studies involving 6993 patients found more treatment responders than placebo (RR 1.53, 95% CI 1.19 to 1.97) and no significant difference versus antidepressants in mild-to-moderate depression, with fewer adverse events than antidepressants (OR 0.67, 95% CI 0.56 to 0.81) [4]. A 2023 meta-analysis of 14 clinical trials likewise supported reduced HAMD burden and a lower side-effect burden relative to SSRIs [5].

For 5-HTP, the 2020 systematic review and meta-analysis reported a pooled remission rate of 0.65 and a large Hedges' g of 1.11, but the underlying studies were heterogeneous and frequently methodologically weak [6]. Accordingly, 5-HTP should be interpreted as a potentially useful serotonergic contributor rather than a stand-alone high-certainty clinical anchor.

Joint-domain human evidence was also directionally supportive. The classic meta-analysis of SAMe in osteoarthritis concluded that SAMe appears as effective as NSAIDs in reducing pain and improving function, with fewer adverse effects [7]. The Cochrane review of chondroitin found a small-to-moderate short-term benefit versus placebo, corresponding to an approximately 8-point greater improvement in pain on a 0-100 scale [8].

3.1. Emotional-support comparative results

Table 3. Emotional-support comparative results in the forced-swimming model.

Group	Immobility time (s)	Change vs blank
Blank control	215.6 ± 18.3	—
Embodiment 1	115.3 ± 12.1	-46.5%
Embodiment 2	128.4 ± 13.5	-40.4%
Embodiment 3	108.7 ± 11.2	-49.6%
Embodiment 4	118.2 ± 12.8	-45.2%
Embodiment 5	120.5 ± 13.0	-44.1%
Comparator example 1	142.8 ± 14.6	-33.8%

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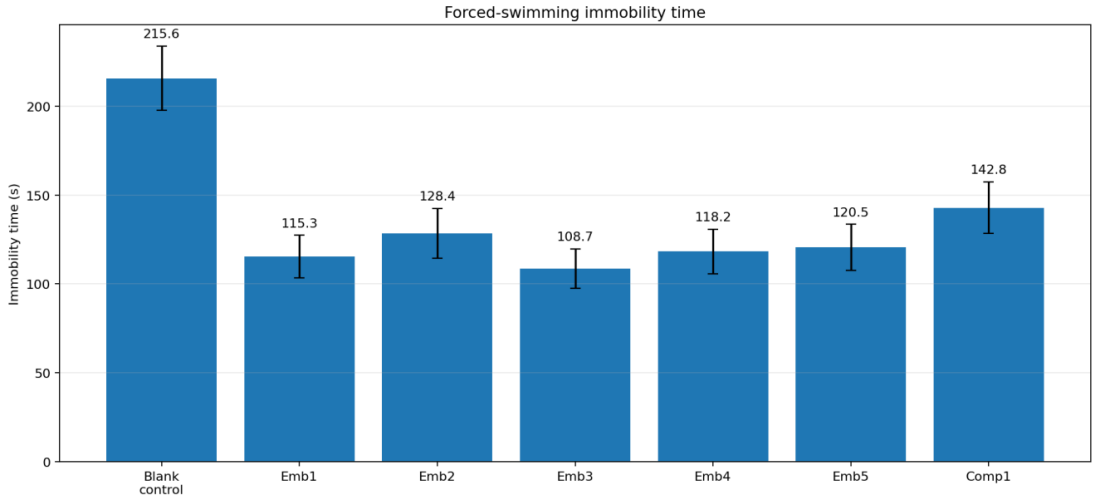

Figure 2. Forced-swimming immobility times across disclosed emotional-support groups.

3.2. Joint-care comparative results

Table 4. Joint-care comparative results in the disclosed osteoarthritis model.

Group	Cartilage matrix synthesis (cpm/mg)	Synovial fluid viscosity (mPa·s)
Sham-operated	1245 ± 98	12.8 ± 1.1
Model	568 ± 72	5.6 ± 0.8
Embodiment 1	1056 ± 85	10.9 ± 0.9
Embodiment 2	987 ± 79	10.1 ± 0.8
Embodiment 3	1089 ± 91	11.2 ± 1.0
Embodiment 4	1043 ± 82	10.7 ± 0.9
Embodiment 5	1038 ± 84	10.6 ± 0.9
Comparator example 1	721 ± 68	7.2 ± 0.7

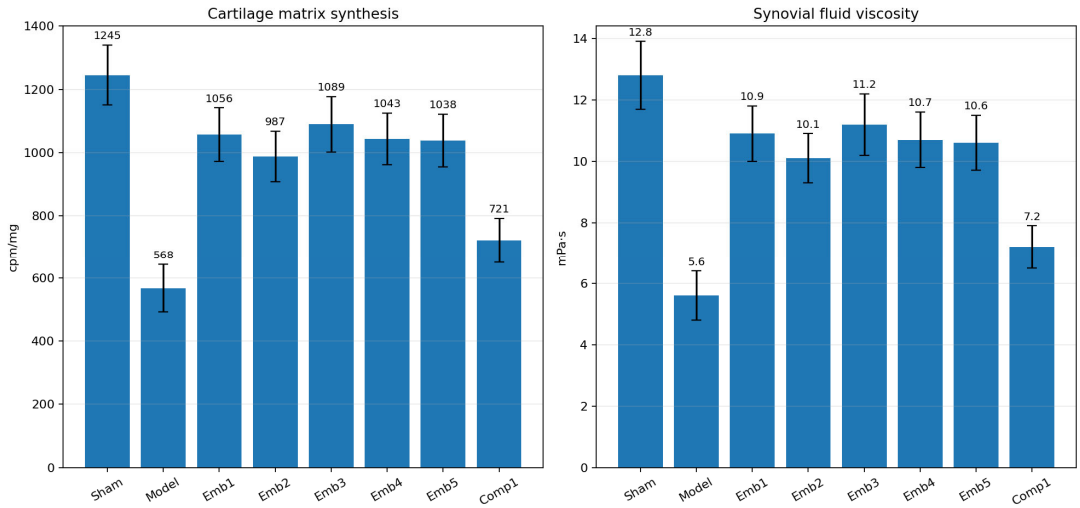

Figure 3. Cartilage matrix synthesis and synovial fluid viscosity in the disclosed osteoarthritis model.

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3.3. Published human clinical evidence anchors

Table 5. Published human clinical evidence anchors for the principal active ingredients.

Ingredient / domain	Evidence base	Key message
SAMe (depression)	2024 meta-analysis, 23 trials, N=2183	Superior to placebo as monotherapy: SMD -0.58 (95% CI -0.93 to -0.23); not significantly different from antidepressants
SAMe (depression)	2024 meta-analysis, 14 trials, N=1522	Symptom relief broadly comparable to imipramine/escitalopram; pooled differences versus comparators not significant
St. John's wort	2016 systematic review, 35 studies, N=6993	More responders than placebo: RR 1.53; not significantly different from antidepressants in mild-to-moderate depression; fewer adverse events
5-HTP	2020 systematic review/meta-analysis, 13 studies	Pooled remission rate 0.65 and Hedges' g 1.11; evidence limited by heterogeneity and weak designs
SAMe (osteoarthritis)	2002 meta-analysis, 11 studies	Comparable to NSAIDs for pain/function, with fewer adverse effects
Chondroitin	2015 Cochrane review	Small-to-moderate short-term benefit; ~8-point greater pain improvement on 0-100 scale

4. Discussion

The main strength of the disclosed composition is not that each single ingredient is individually novel, but that the formula is organized to cover two clinically relevant domains that commonly overlap in real-world supplement use: emotional support and joint care. SAMe provides the clearest bridge between those domains because it appears in both the depression and osteoarthritis evidence base.

The disclosed comparator data are especially informative because the comparator retained the emotional-support core while removing the joint-care synergists. The fact that the full formula preserved or improved emotional-support performance while materially improving osteoarthritis-related metrics argues against simple ingredient crowding and supports genuine formula-level synergy.

At the same time, the clinical literature imposes clear boundaries. SAMe and St. John's wort have the most credible human evidence in the mood domain, whereas 5-HTP remains promising but less certain. Chondroitin offers the most robust over-the-counter joint-support anchor among the joint-care adjuncts included here. Oral sodium hyaluronate, vitamin B6, vitamin E, and phosphatidylserine are mechanistically plausible contributors, but they are not the strongest independent drivers of the clinical narrative.

Safety and medication interaction assessment are essential. St. John's wort interacts with many prescription drugs and can weaken the effects of oral contraceptives, warfarin, digoxin, cyclosporine, some statins, some HIV agents, and other therapies. In addition, combining St. John's wort with certain antidepressants or other serotonergic agents can increase serotonin-related adverse effects [9-10]. Because this composition also includes SAMe and 5-HTP, clinical positioning should emphasize medication review and cautious use rather than indiscriminate combination with prescription antidepressants.

The principal limitation is that direct human superiority of the exact finished composition over competing finished products has not yet been established in a source-verified randomized trial. The present paper therefore supports a clinically credible development narrative rather than a

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finalized therapeutic claim. The next scientific step should be a registered, double-blind, active-comparator trial using validated depression, sleep, pain, WOMAC, and rescue-medication endpoints.

5. Conclusion

We conclude that the disclosed SAMe-5-HTP-Hypericum compound supplement has a persuasive translational profile for dual-domain emotional support and joint care. Within the disclosed comparator framework, the full formula outperformed the reduced comparator in both forced-swimming and osteoarthritis-related outcomes, with the upper-limit formulation showing the strongest overall performance.

When these comparative data are aligned with published human clinical evidence, SAMe and St. John's wort emerge as the strongest clinical anchors for the emotional-support domain, while SAMe and chondroitin sulfate support the joint-care domain. The formula therefore has a stronger evidence architecture than many single-purpose supplements. A direct randomized clinical trial of the finished composition is now warranted to convert this translational case into a fully confirmatory clinical dossier.

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