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BCLC™ NAD+ Supplement System Targeting SIRT1: A Time-Sequential Biphasic NMN-Resveratrol-Quercetin Formulation with Supporting Clinical and Pharmacological Evidence

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ABSTRACT

Background: Age-associated decline in NAD+ is closely linked to reduced SIRT1 activity and impaired metabolic resilience. The disclosed BCLC™ system combines NMN, trans-resveratrol, quercetin, piperine, and trimethylglycine within a time-sequential biphasic release architecture. Objective: We retained the disclosed composition, formulation parameters, figures, and performance data, and further matched them with published human and mechanistic evidence relevant to the system modules. Methods: We summarized the disclosed active-component window, release design, and in-vitro endpoints, and compared them with peer-reviewed studies on NMN, resveratrol, quercetin, piperine, methyl-donor metabolism, and cyclodextrin-based solubility engineering. Results: The disclosed system outperformed a conventional comparator in reported cell and dissolution endpoints, including 4.1-5.5-fold SIRT1-pathway activation, 95.6-98.8% nicotinamide clearance, >=36-48 h intracellular NAD+ maintenance, and markedly improved 15-min dissolution of resveratrol, quercetin, and piperine. Published human studies consistently showed that NMN raises blood NAD+ and is generally well tolerated, while resveratrol displayed context-dependent metabolic and SIRT1-related effects and quercetin showed selective cardiometabolic and insulin-sensitivity benefits. Human evidence supporting piperine and methyl-donor support was indirect but mechanistically relevant. Conclusion: We consider the disclosed BCLC™ architecture biologically plausible and better supported than a simple mixed formulation.

KEYWORDS

NAD+; NMN; SIRT1; Resveratrol; Quercetin; Piperine; Trimethylglycine; Biphasic release; Cyclodextrin; Formulation science

1. INTRODUCTION

We developed the present manuscript around a disclosed NAD+-support formulation system that couples an immediate NMN phase with a delayed intestinal phase carrying polyphenol and excipient modules. [1] Rather than treating the formula as a simple ingredient mixture, we evaluated it as a coordinated delivery architecture centered on temporal exposure, solubility engineering, absorption support, and methyl-balance support.

NAD+ availability is tightly linked to the activity of SIRT1 and other NAD+-consuming enzymes, and recent human intervention studies have made NAD+-raising strategies a realistic translational topic. [2-5] At the same time, the published literature shows that efficacy is highly context-dependent: benefits observed in metabolically stressed or older populations are not always reproduced in healthier cohorts, especially for polyphenols such as resveratrol and quercetin [6-11].

For that reason, we did not rewrite the disclosed system as a promotional narrative. Instead, we retained the disclosed tables and figures, then compared those data against published clinical and mechanistic findings to judge whether the formulation logic is coherent, where the evidence is strongest, and where the evidence remains incomplete.

2. MATERIALS AND METHODS

2.1. Disclosed Composition and Formulation Modules

The disclosed system defines an active composition window totaling 100 parts by weight and uses a biphasic release ratio of 1:(4-6) between the immediate-release and enteric sustained-release synchronous phases. [1] In the present manuscript, we preserved these core quantitative settings and the original figure order.

Table 1. Disclosed active-ingredient composition window and system roles

Component	Parts by weight (total actives = 100)	Role in the disclosed system
β-Nicotinamide mononucleotide (NMN)	30-60	Primary NAD+ precursor; configured in immediate and sustained fractions
trans-Resveratrol	8-20	Polyphenol intended to support SIRT1-related signaling
Quercetin (aglycone)	2-10	Polyphenol intended to support NAD+ homeostasis and oxidative-stress control
Piperine (black pepper extract)	0.5-3	Absorption-support module for poorly soluble polyphenols
Trimethylglycine (betaine)	Balance	Methyl-donor support; proposed to buffer nicotinamide-related methyl burden

Table 2. Key formulation modules and disclosed parameters

Design element	Implementation	Key parameters disclosed
Biphasic time-sequential release	Immediate-release phase + enteric sustained-release synchronous phase	IR:enteric SR sync = 1:(4-6)
Inclusion complex	Resveratrol + quercetin + piperine in HP-β-CD	HP-β-CD DS 4-9; mass ratio 4-8:1
Sustained-release / enteric materials	Hypromellose K4M; acrylic resin II/III	K4M 3-8% of enteric phase; coating gain 3-8%

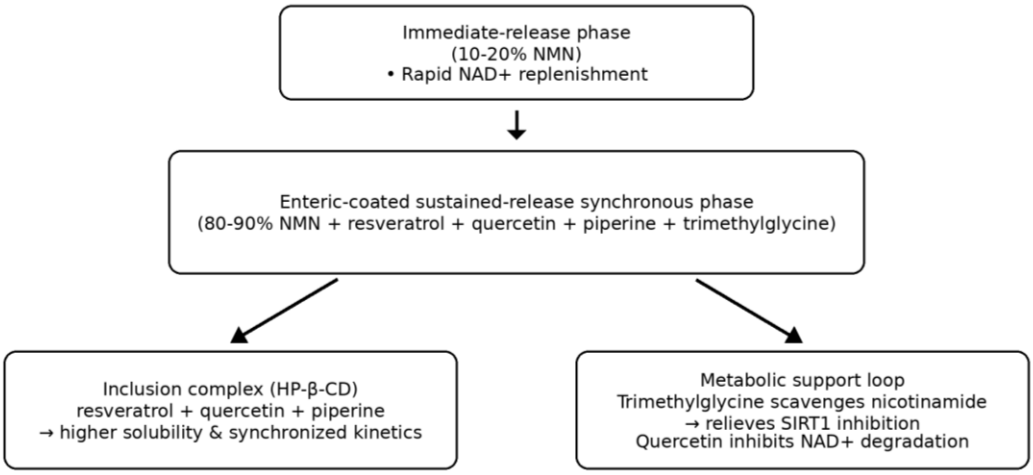

Figure 1. Conceptual illustration of the time-sequential biphasic release design retained from the disclosed system.

2.2. Published Evidence Appraisal Strategy

We then examined peer-reviewed published studies relevant to each functional module of the system: NMN as the NAD+ precursor; resveratrol and quercetin as polyphenol partners; piperine as an absorption-support excipient; trimethylglycine as a methyl-donor support component; and HP-β-CD as a solubility-enhancing complexation strategy. [2-14] Priority was given to controlled human intervention studies and directly relevant mechanistic or formulation papers.

The principal retained performance endpoints from the disclosed system were SIRT1-pathway activation, nicotinamide clearance, intracellular NAD+ maintenance, dissolution behavior under simulated gastric and intestinal conditions, active-retention stability, and material loss during preparation [1].

3. RESULTS

3.1. Performance Retained from the Disclosed System

The disclosed system reported a consistent advantage over the conventional comparator across all three embodiments. SIRT1-pathway activation ranged from 4.1- to 5.5-fold above blank, whereas the comparator reached 1.2-fold only. [1] Nicotinamide clearance remained between 95.6% and 98.8%, and intracellular NAD+ maintenance extended to at least 36-48 h, versus <=12 h in the comparator [1].

Dissolution data further supported the delivery rationale. At 15 min, disclosed dissolution of trans-resveratrol, quercetin, and piperine generally exceeded 87-93%, while the comparator remained around 42-45%. [1] The enteric pellets also minimized acidic-medium release and then achieved strong release at intestinal pH, which is directionally consistent with a delayed co-exposure design [1].

Table 3. Summary of retained reported endpoints for the disclosed system

Detection index	Embodiment 1	Embodiment 2	Embodiment 3	Conventional comparator
SIRT1 pathway activation (fold vs blank)	5.2-fold	4.1-fold	5.5-fold	1.2-fold
Nicotinamide clearance rate (%)	98.3	95.6	98.8	0
Intracellular NAD+ maintenance time (h)	>=48	>=36	>=48	<=12
Trans-resveratrol 15-min dissolution (%)	92.5	89.2	93.1	45.2
Quercetin 15-min dissolution (%)	90.8	87.5	91.5	41.8
Piperine 15-min dissolution (%)	91.2	88.3	92.6	43.5
Enteric pellet 2-h dissolution at pH 1.2 (%)	<=2.8	<=3.2	<=2.5	No enteric pellets
Enteric pellet 4-h dissolution at pH 6.8 (%)	88.6	85.3	90.2	Irregular release
Active retention after 3 months (%)	98.5	97.8	98.2	65.3
Formulation stability at 3 months	No degradation/ layering/adhesion	No degradation/ layering/ adhesion	Slight adhesion; usable	Degradation, layering, caking
Material loss during preparation (%)	<=3	<=3.5	<=3	>=18

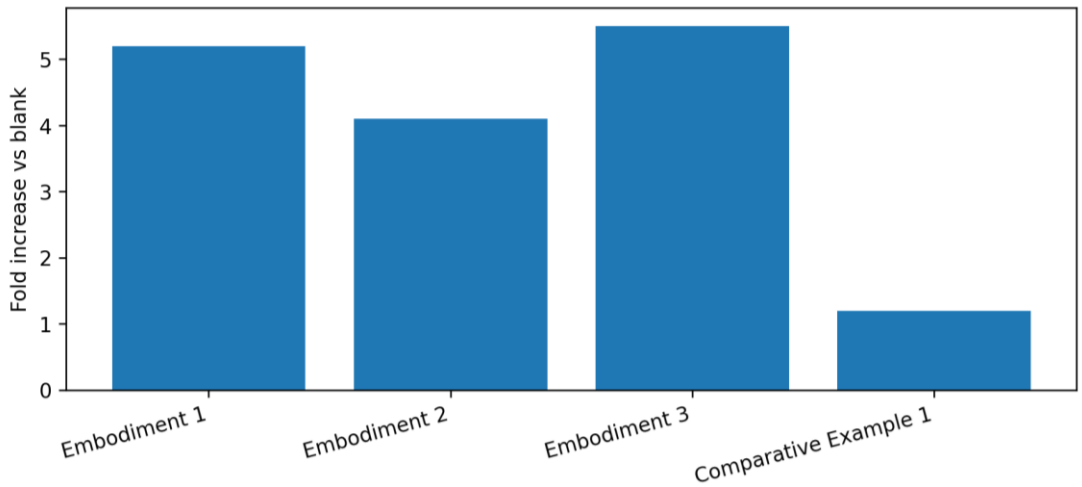

Figure 2. Retained in-vitro SIRT1 pathway activation results of the disclosed system

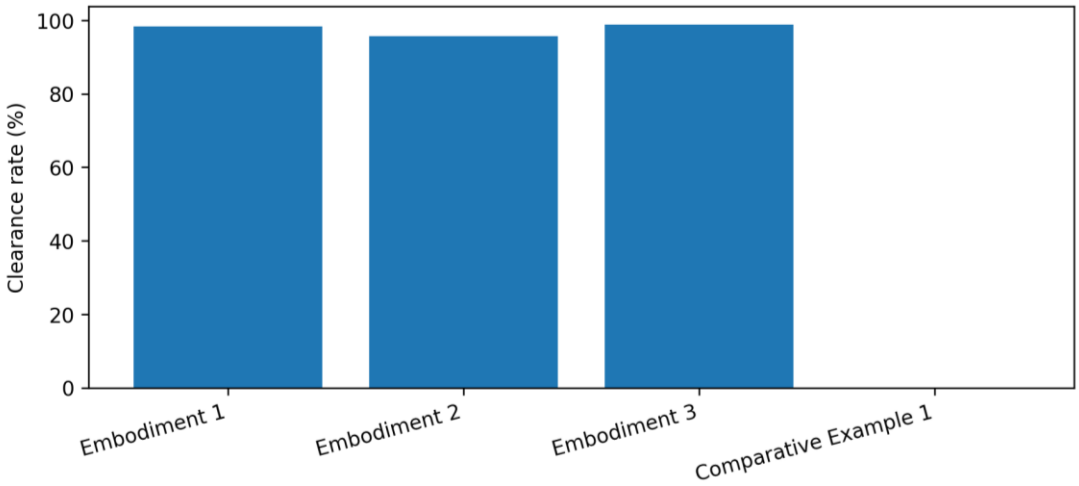

Figure 3. Retained in-vitro nicotinamide clearance results of the disclosed system

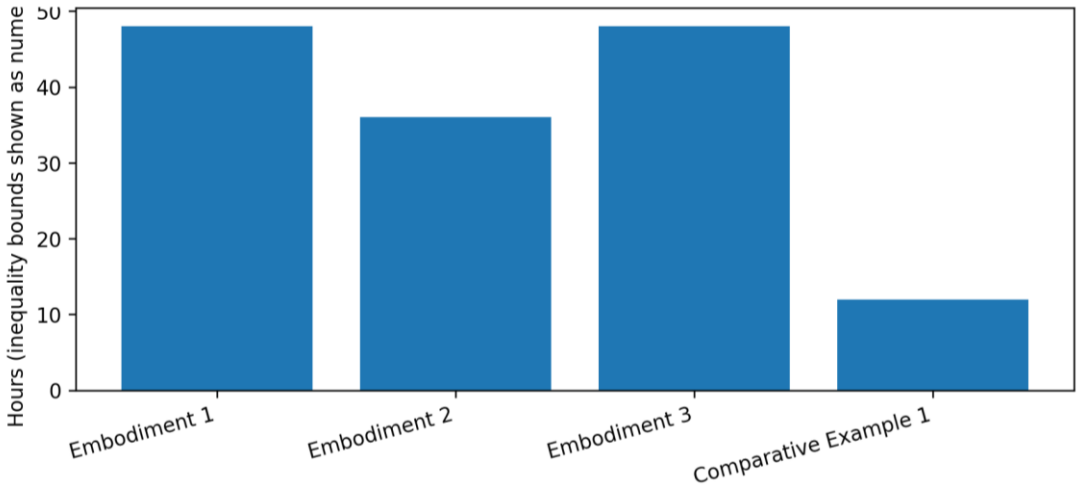

Figure 4. Retained intracellular NAD+ maintenance results of the disclosed system

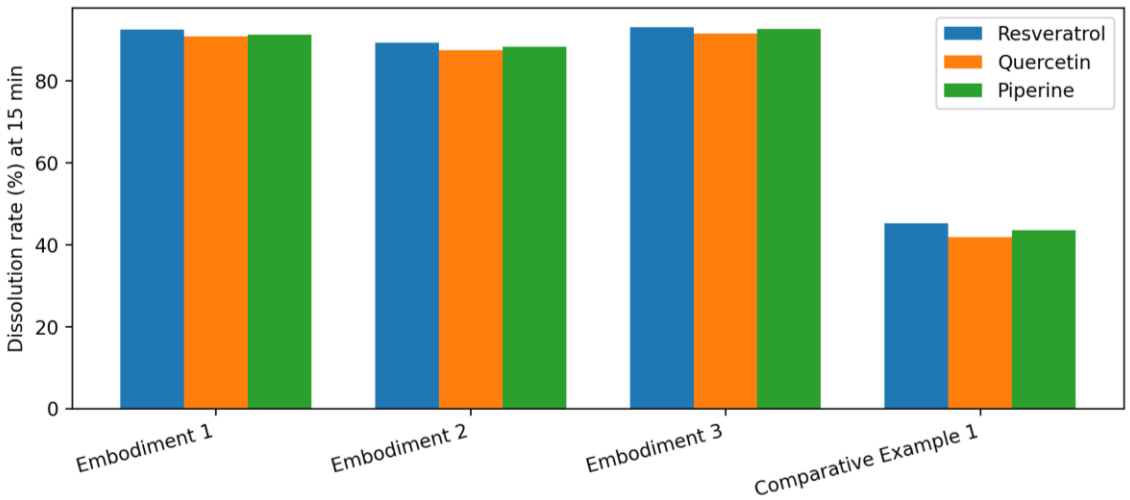

Figure 5. Retained 15-min dissolution results for poorly soluble components

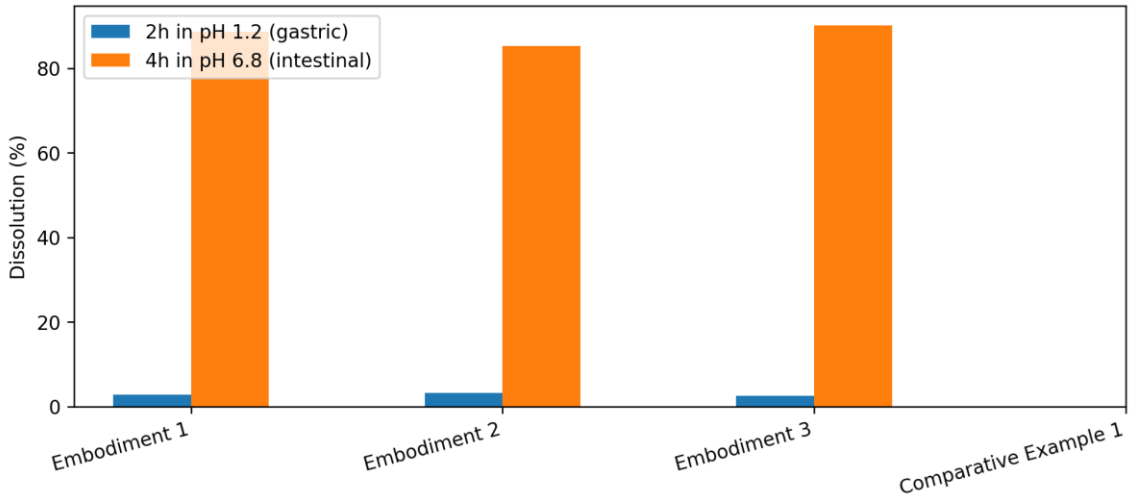

Figure 6. Retained enteric sustained-release control results under pH 1.2 and pH 6.8 conditions

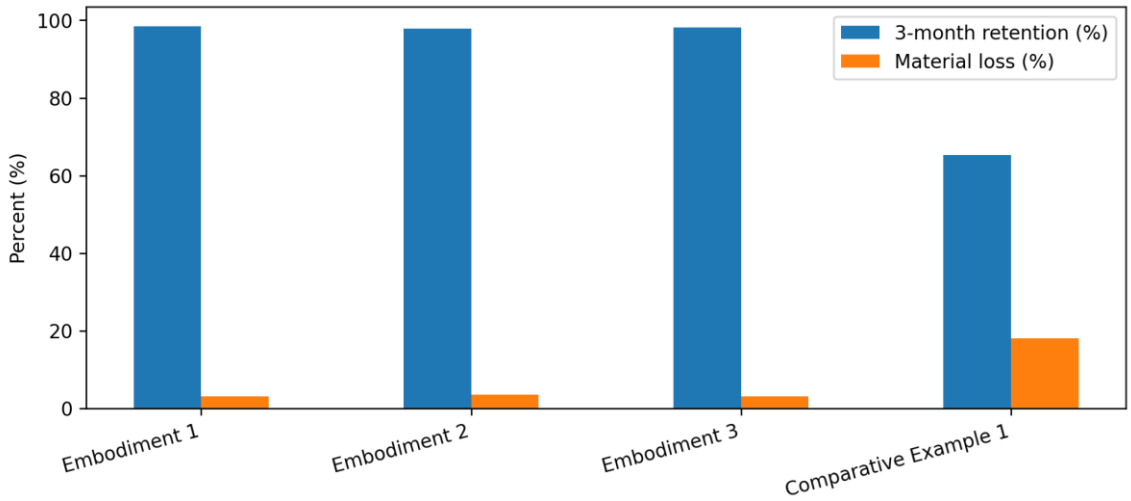

Figure 7. Retained 3-month active-retention and material-loss results

3.2. Published Human and Formulation Evidence Relevant to Each Module

Published human evidence most strongly supports the NMN module. A 10-week randomized placebo-controlled trial in overweight or obese postmenopausal women with prediabetes found improved muscle insulin sensitivity and insulin signaling after 250 mg/day NMN. [2] A separate 12-week placebo-controlled trial in healthy adults showed that 250 mg/day NMN increased whole-blood NAD+ without obvious adverse effects, [3] and a multicenter dose-ranging trial in 80 middle-aged adults demonstrated dose-dependent NAD+ increases with the clearest functional gain at 600 mg/day in the six-minute walk test. [4] More recently, 250 mg/day for 12 weeks in older adults increased blood NAD+ metabolites, maintained walking speed, and improved sleep-quality scores [5].

For the resveratrol module, the published record was mixed rather than uniformly positive. In healthy obese men, 150 mg/day for 30 days activated AMPK, increased SIRT1 and PGC-1α protein levels, and improved several metabolic endpoints. [6] However, 75 mg/day for 12 weeks in nonobese postmenopausal women produced no metabolic benefit and did not alter SIRT1-related molecular targets. [7] In a separate randomized trial in adults aged 55-65 years, 500 mg/day for 30 days significantly increased serum Sirt1 concentrations, indicating that a SIRT1-related systemic signal can be detected in humans under some conditions [8].

Table 4. Published studies relevant to the disclosed BCLC™ system

Module / ingredient	Published study design	Dose and population	Main published finding
NMN	Randomized, double-blind, placebo-controlled trial [2]	250 mg/day for 10 weeks; overweight/obese postmenopausal women with prediabetes	Improved muscle insulin sensitivity and insulin signaling versus placebo
NMN	Randomized, double-blind, parallel-group trial [3]	250 mg/day for 12 weeks; 30 healthy adults	Raised whole-blood NAD+ with no obvious adverse effects
NMN	Multicenter randomized dose-ranging trial [4]	300/600/900 mg/day for 60 days; 80 healthy middle-aged adults	Dose-dependent increase in blood NAD+; 6-minute walk distance improved; safety profile acceptable
NMN	Double-blind randomized placebo-controlled trial [5]	250 mg/day for 12 weeks; older adults	Higher blood NAD+ and metabolites; shorter 4-m walking time; improved sleep-quality scores
Resveratrol	Randomized double-blind crossover trial [6]	150 mg/day for 30 days; 11 healthy obese men	Activated AMPK, increased SIRT1/PGC-1α protein levels, and improved several metabolic endpoints
Resveratrol	Randomized placebo-controlled trial [7]	75 mg/day for 12 weeks; nonobese postmenopausal women	No improvement in insulin sensitivity or SIRT1-related molecular targets
Resveratrol	Randomized trial [8]	500 mg/day for 30 days; 48 healthy adults aged 55-65 years	Serum Sirt1 concentration increased significantly after intervention
Resveratrol + piperine	Randomized double-blind cross-over trial [9]	250 mg resveratrol +/- 20 mg piperine; 23 adults	Co-supplementation augmented task-related cerebral blood flow, but plasma resveratrol and cognition were unchanged
Quercetin	Randomized double-blind cross-over trial [10]	162 mg/day for 6 weeks; 70 overweight-to-obese patients with (pre-)hypertension	Lowered ambulatory systolic blood pressure in the hypertensive subgroup; no broad endothelial or inflammatory effect
Quercetin	Randomized placebo-controlled double-blind trial [11]	1 g/day for 12 weeks; 84 women with PCOS	Improved adiponectin-mediated insulin sensitivity and hormonal profile
Betaine / methyl-donor support	Controlled clinical trial [12] plus mechanistic NNMT study [13]	1.5-6 g/day for 6 weeks in healthy adults; mechanistic hepatic model	Betaine lowered homocysteine dose-dependently; NNMT consumed methyl donors and interacted with methionine-cycle enzymes, supporting a methyl-balance rationale rather than proving nicotinamide 'scavenging'
HP-β-CD inclusion complex	Formulation study [14]	Quercetin-HP-β-CD spray-dried complex	Approximately 8-fold higher quercetin dissolution in simulated gastric fluid

Quercetin also showed selective rather than universal benefit. In overweight-to-obese patients with (pre-) hypertension, 162 mg/day for 6 weeks lowered ambulatory systolic blood pressure in the hypertensive subgroup but did not broadly improve endothelial or inflammatory markers. [10] In women with polycystic ovary syndrome, 1 g/day for 12 weeks improved adiponectin-mediated insulin sensitivity and the hormonal profile [11].

For the support modules, the evidence was more mechanistic. An acute randomized cross-over trial found that adding 20 mg piperine to 250 mg resveratrol augmented task-related cerebral blood flow, although plasma resveratrol concentrations and cognition were unchanged, indicating physiological modulation without clear pharmacokinetic amplification in that specific human setting. [9] Separately, a controlled clinical trial showed that betaine lowered fasting and post-methionine-loading homocysteine dose-dependently, [12] while an NNMT mechanistic study showed that nicotinamide methylation consumes methyl donors and interacts with methionine-cycle enzymes. [13] Finally, a formulation study showed that a quercetin-HP-β-CD complex increased quercetin dissolution approximately eightfold in simulated gastric fluid, directly supporting the disclosed solubility-engineering logic [14].

4. DISCUSSION

When we place the disclosed system data next to the published literature, the strongest external support clearly resides in the NMN module and in the general rationale for improving polyphenol delivery. The human NMN trials consistently point in the same direction for blood NAD+ elevation and short-term tolerability, [3-5] which makes the precursor core of the system more credible than the downstream synergy claims.

The resveratrol and quercetin data argue for nuance. We interpret the literature as showing that these polyphenols can contribute measurable biological effects in selected metabolic contexts, but that those effects are not robustly universal across populations or endpoints. [6-11] For that reason, the disclosed formulation should not be interpreted as clinically validated merely because its components each have published activity.

The excipient and support modules are important to the formulation logic, but they should also be described precisely. Based on the published evidence, piperine is best framed as a physiological or absorption-support modulator rather than as a guaranteed bioavailability amplifier in every human setting. [9] Similarly, trimethylglycine is better justified as methyl-donor support in the context of nicotinamide methylation pressure, not as definitive proof of direct nicotinamide scavenging in humans [12, 13].

Our overall reading is therefore balanced. The disclosed BCLC™ system is more scientifically coherent than a conventional unstructured blend because it combines timed release, solubility engineering, and metabolic-support concepts within one architecture. [1, 14] At the same time, no published registered human trial directly testing this exact time-sequential composite was identified. The next decisive step should be a randomized controlled clinical study with prespecified pharmacokinetic, NAD+-metabolome, safety, and functional endpoints.

5. CONCLUSIONS

In summary, we found that the disclosed BCLC™ system presents a technically coherent formulation strategy in which biphasic release, HP-β-CD complexation, piperine support, and methyl-balance support are organized around an NMN-centered NAD+-raising core. The retained disclosed data suggest superior in-vitro and dissolution performance relative to a conventional comparator, while published human studies provide meaningful but partial support for the biological roles of the individual modules. [1-14] The complete clinical efficacy of the exact BCLC™ composite remains to be established by direct human trials.

REFERENCES

[1] BCLC™ NMN Composite Anti-Aging Formulation for Activating the SIRT1 Pathway and a Preparation Thereof. Source formulation disclosure/manuscript, 2026.

[2] Yoshino M, Yoshino J, Kayser BD, et al. Nicotinamide mononucleotide increases muscle insulin sensitivity in prediabetic women. Science. 2021; 372(6547):1224-1229. doi:10.1126/science.abe9985.

[3] Okabe K, Yaku K, Uchida Y, et al. Oral Administration of Nicotinamide Mononucleotide Is Safe and Efficiently Increases Blood Nicotinamide Adenine Dinucleotide Levels in Healthy Subjects. Front Nutr. 2022; 9:868640. doi:10.3389/fnut.2022.868640.

[4] Yi L, Maier AB, Tao O, et al. The efficacy and safety of β-nicotinamide mononucleotide (NMN) supplementation in healthy middle-aged adults: a randomized, multicenter, double-blind, placebo-controlled, parallel-group, dose-dependent clinical trial. Geroscience. 2023; 45(1):29-43. doi:10.1007/s11357-022-00705-1.

[5] Morifuji M, Sato D, Odagiri H, et al. Ingestion of β-nicotinamide mononucleotide increased blood NAD levels, maintained walking speed, and improved sleep quality in older adults in a double-blind randomized, placebo-controlled study. Geroscience. 2024; 46(5):4671-4688. doi:10.1007/s11357-024-01171-0.

[6] Timmers S, Auwerx J, Schrauwen P. Calorie restriction-like effects of 30 days of resveratrol supplementation on energy metabolism and metabolic profile in obese humans. Cell Metab. 2011; 14(5):612-622. doi:10.1016/j.cmet.2011.10.002.

[7] Yoshino J, Conte C, Fontana L, et al. Resveratrol supplementation does not improve metabolic function in nonobese women with normal glucose tolerance. Cell Metab. 2012; 16(5):658-664. doi:10.1016/j.cmet.2012.09.015.

[8] Mansur AP, Roggerio A, Goes MFS, et al. Serum concentrations and gene expression of sirtuin 1 in healthy and slightly overweight subjects after caloric restriction or resveratrol supplementation: A randomized trial. Int J Cardiol. 2017; 227:788-794. doi:10.1016/j.ijcard.2016.10.058.

[9] Wightman EL, Reay JL, Haskell CF, et al. Effects of resveratrol alone or in combination with piperine on cerebral blood flow parameters and cognitive performance in human subjects: a randomised, double-blind, placebo-controlled, cross-over investigation. Br J Nutr. 2014; 112(2):203-213. doi:10.1017/S0007114514000737.

[10] Brüll V, Burak C, Stoffel-Wagner B, et al. Effects of a quercetin-rich onion skin extract on 24 h ambulatory blood pressure and endothelial function in overweight-to-obese patients with (pre-)hypertension: a randomised double-blinded placebo-controlled cross-over trial. Br J Nutr. 2015; 114(8):1263-1277. doi:10.1017/S0007114515002950.

[11] Rezvan N, Moini A, Janani L, et al. Effects of Quercetin on Adiponectin-Mediated Insulin Sensitivity in Polycystic Ovary Syndrome: A Randomized Placebo-Controlled Double-Blind Clinical Trial. Horm Metab Res. 2017; 49(2):115-121. doi:10.1055/s-0042-118705.

[12] Olthof MR, van Vliet T, Boelsma E, Verhoef P. Low dose betaine supplementation leads to immediate and long term lowering of plasma homocysteine in healthy men and women. J Nutr. 2003; 133(12):4135-4138. doi:10.1093/jn/133.12.4135.

[13] Hong S, Zhai B, Pissios P. Nicotinamide N-Methyltransferase Interacts with Enzymes of the Methionine Cycle and Regulates Methyl Donor Metabolism. Biochemistry. 2018; 57(40):5775-5779. doi:10.1021/acs.biochem.8b00561.

[14] Zheng Y, Chow AHL. Production and characterization of a spray-dried hydroxypropyl-beta-cyclodextrin/quercetin complex. Drug Dev Ind Pharm. 2009; 35(6):727-734. doi:10.1080/03639040802526805.