Randomized Controlled Trial

Evaluating the Efficacy of GCSB-5 in Lumbar Disc Herniation: A Randomized Controlled Trial

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Background: GCSB-5 has demonstrated a favorable safety profile and promising efficacy in reducing pain, exerting anti-inflammatory effects, and improving joint function in patients with osteoarthritis.

Objectives: To evaluate the clinical effectiveness and safety of GCSB-5, a botanical formulation known for its anti-inflammatory and analgesic properties, in patients with lumbar disc herniation.

Study Design: Double-blinded, placebo-controlled design.

Setting: Two university hospitals in the Republic of Korea.

Methods: This prospective, multicenter, double-blinded, randomized, placebo-controlled clinical trial was conducted over 16 weeks. In total, 46 patients with lumbar disc herniation were enrolled and randomly assigned to either the GCSB-5 group (n = 23) or the placebo group (n = 23). The GCSB-5 and placebo tablets were administered for 12 weeks. The primary outcome was the change in Numeric Rating Scale (NRS-11) scores for back pain from baseline to post treatment commencement week 16. Secondary outcomes included NRS-11 changes in radiating leg pain, Oswestry Disability Index scores, Short Form-36 scores, and magnetic resonance imaging-based structural assessments. Adverse events were monitored throughout the study.

Results: One patient in the GCSB-5 group and 4 patients in the placebo group dropped out. The GCSB-5 group showed a statistically significant greater reduction in NRS-11 scores for back pain compared to the placebo group at post treatment commencement weeks 4, 8, and 16. Additionally, leg pain was statistically improved more significantly in the GCSB-5 group at post treatment commencement weeks 4, 8, 12, and 16. Functional outcomes, as assessed by the Oswestry Disability Index, had a statistically significant greater reduction in the GCSB-5 group at post treatment commencement week 16. However, magnetic resonance imaging analyses revealed no statistically significant difference between the 2 groups. No serious adverse events were reported, and the safety profile of GCSB-5 was comparable to that of the placebo.

Limitations: The short study duration.

Conclusion: Our study suggests that GCSB-5 may reduce pain in patients with lumbar disc herniation, with potential improvement in functional ability and mental well-being. Further large-scale studies are needed to validate these findings.

Key words: Lumbar disc herniation, GCSB-5; pain, function

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Lumbar disc herniation (LDH) is a common medical condition characterized by axial and radiating back pain (1,2) that primarily results from mechanical compression or chemical irritation of the affected nerve (3). LDH not only substantially impairs a patient's quality of life, it also imposes a substantial

socioeconomic burden due to functional impairments and high health care costs. Despite various treatment options—including physical therapy, pharmacological interventions, and surgical options—managing LDH is a clinical challenge. The long-term use of conventional analgesics, such as nonsteroidal anti-inflammatory drugs and opioids, is often associated with considerable adverse effects, including gastrointestinal and cardiovascular complications (4,5), highlighting the need for safer and more effective alternatives. Moreover, the ongoing opioid crisis further emphasizes the necessity for alternative pain management strategies (6,7). Thus, there is a pressing demand for analgesics that are both effective and safe.

GCSB-5 (GC Pharma) is a herbal formulation approved in the Republic of Korea for managing joint-related conditions (8). Comprising 6 herbal ingredients (Ledebouriellae radix, Achyranthis radix, Acanthopanacis cortex, Cibotii rhizoma, Glycini semen, and Eucommiae cortex) (8), GCSB-5 has demonstrated a favorable safety profile and promising efficacy in reducing pain, exerting anti-inflammatory effects, and improving joint function in patients with osteoarthritis (9,10). These properties suggest that GCSB-5 may also be effective for treating other inflammatory and chronic pain conditions such as LDH (11,12). This medication is currently only used in the Republic of Korea. Although research on GCSB-5 in disc diseases is ongoing (13,14), its well-established anti-inflammatory effects position it as a potential therapeutic option for addressing underlying inflammation in LDH.

The pathophysiology of LDH is primarily driven by inflammation resulting from intervertebral disc degeneration. Given GCSB-5's proven anti-inflammatory properties, it is hypothesized that this herbal formulation can effectively target the inflammatory mechanisms underlying LDH, thereby providing therapeutic benefits.

Our prospective, multicenter, double-blinded, randomized, placebo-controlled clinical trial aimed to evaluate the efficacy and safety of GCSB-5 in patients with LDH compared to a placebo over a 12-week treatment period. By investigating its effect on pain relief and functional recovery, we aimed to establish GCSB-5 as a viable treatment option for LDH, thereby expanding its therapeutic application and enhancing patient management strategies.

Methods

Ethical Considerations

Our study was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki and adhered to Good Clinical Practice guidelines. Institutional Review Board approvals were obtained from all participating centers (IRB No. 4-2017-0378, NS17-02). Written informed consent was obtained from all patients prior to enrollment.

Study Design

Our study was a prospective, multicenter, double-blinded, randomized, placebo-controlled clinical trial conducted at 2 university hospitals from July 1, 2017 through April 30, 2018, spanning a total duration of 16 weeks. Its objective was to evaluate the efficacy and safety of GCSB-5 in patients diagnosed with LDH. Eligible patients were randomized to receive either GCSB-5 or a placebo over a 12-week treatment period. They had follow-up visits every 4 weeks post treatment commencement for a total of 16 weeks. The primary objective was to assess their reduction in back pain, as measured by changes in the Numeric Rating Scale (NRS-11) score, from baseline to post treatment commencement week 16. Secondary objectives included evaluating the reduction in leg pain using the NRS-11 score, improvements in functional disability using the Oswestry Disability Index (ODI), enhancements in quality of life as measured by the Short Form-36 (SF-36) questionnaire, and the incidence and severity of adverse events throughout the study period.

Study Population

The patients were all adults aged 19–60 years who had been diagnosed with LDH based on clinical symptoms and magnetic resonance imaging (MRI) findings within 6 months prior to enrollment. Eligible patients reported a pre-enrollment NRS-11 pain score of ≥ 4 for either back or leg pain.

Exclusion criteria included using medications that could confound efficacy evaluations (e.g., nonsteroidal anti-inflammatory drugs, opioids, muscle relaxants) or having received interventions within the preceding 3 months—such as epidural steroid injections, nerve root blocks, or other treatments—that could confound outcomes. Additional exclusions were applied to those diagnosed with trauma-related LDH, psychiatric disorders requiring medication, active peptic ulcers, gastrointestinal bleeding, inflammatory bowel disease, severe hepatic or renal impairment, congestive heart failure, clinically significant ischemic heart disease, peripheral arterial disease, or cerebrovascular disease. Those with a history of esophageal or gastric

ulcers within the preceding year or bleeding disorders (e.g., platelet abnormalities or coagulation factor deficiencies) were also excluded. Those with a history of gastrointestinal surgery (except appendectomy), or with screening laboratory values for serum creatinine, alanine aminotransferase, aspartate aminotransferase, or total bilirubin levels exceeding 1.5 times the upper limit of normal were deemed ineligible. The final exclusion criteria included participation in another clinical trial within 4 weeks prior to enrollment, pregnancy or lactation, a history of malignancy within the preceding 5 years, and women of childbearing potential who did not agree to use effective contraception (e.g., sterilization, oral contraceptives, intrauterine devices, condoms, or barrier methods with spermicidal agents) during the study period.

Sample size was calculated based on data from a previous clinical trial (NCT01535417). When we adopted a Type I error of 0.05, a power of 80%, and a 2-sided test, 19 patients per group were required. Accounting for a 20% dropout rate, the final recruitment target was 23 patients per group (12 from one hospital and 11 from the other hospital) (Fig. 1).

Randomization and Blinding

Eligible patients who provided informed consent were randomized in a 1:1 ratio to receive either GCSB-5 or placebo tablets. Randomization was performed using a computer-generated block randomization method, stratified by study site, to ensure balanced group allocation. Patients were assigned sequentially according to the randomization sequence starting from the lowest allocation number. Both the patients and the investigators were blinded to the group allocations. Additionally, the placebo tablets were identical in appearance and physical characteristics to the GCSB-5 tablets to maintain blinding.

Intervention

Patients in the GCSB-5 group received tablets containing 300 mg of GCSB-5 per tablet. The dosing regimen was 2 tablets in the morning and 2 in the evening for a total daily dose of 1,200 mg. The placebo group followed the same dosing schedule with tablets matched in shape, color, and weight to the GCSB-5 tablets. The intervention period lasted 12 weeks. Medication compliance was monitored at each follow-up visit by counting returned tablets. If pain was not adequately controlled during the study period, the use of acetaminophen 650 mg 3 times a day or oxycodone/naloxone, Mundipharma, Germany 5 mg/25 mg twice a day was permitted as rescue medication.

Study Visits and Assessments

Patients attended scheduled visits at baseline and at 4, 8, 12, and 16 weeks after commencing treatment. During these visits, pain intensity was evaluated using the NRS-11 for both back and leg pain, with scores ranging from 0 (no pain) to 10 (worst pain imaginable). Functional ability was measured using the ODI, scored from 0 to 100, with higher scores indicating greater impairment. Quality of life was assessed using the SF-36 questionnaire, which generates a Physical Component Score and a Mental Component Score to measure a patient's physical and mental well-being. Scores ranged from 0 to 100, with higher scores reflecting better health status.

At the final visit (post treatment commencement week 16), lumbar spine MRIs were conducted to evaluate structural changes, including disc dehydration (Pfirrmann grading) (15), disc height, and spinal canal area, which were compared with MRI imaging taken at baseline. Safety assessments, including the incidence and severity of adverse events, were also collected and recorded at each visit.

Primary and Secondary Endpoints

The primary endpoint was the change in NRS-11 scores for back pain from baseline to post treatment commencement weeks 4, 8, 12, and 16. Secondary endpoints included changes in NRS-11 scores for leg pain at each follow-up, changes in ODI and SF-36 scores,

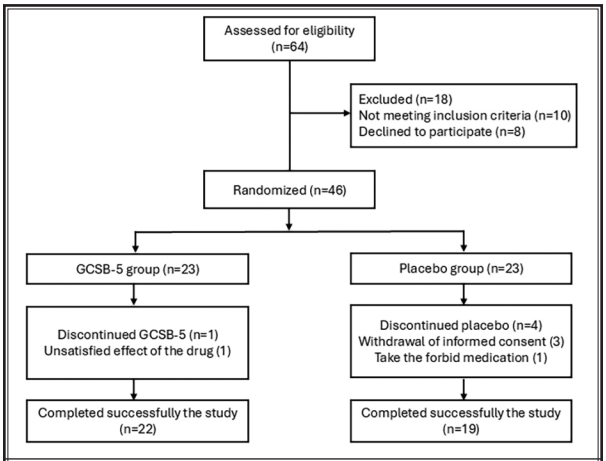

Fig. 1. *CONSORT flowchart showing patient allocation, follow-up, and final study inclusion.*

structural changes observed on MRI, and the frequency and severity of adverse events.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 29.0 (Armonk, NY, USA: IBM Corp.). The normality of the data distribution was assessed using the Kolmogorov–Smirnov test. Intergroup comparisons were conducted using independent t tests. Data from patients who withdrew from the study were excluded from the final analysis.

Results

During the study period, one patients in the GCSB-5 group and 4 in the placebo group dropped out (Fig. 1). Despite this, there were no statistically significant differences between the 2 groups in baseline demographic characteristics, including age, gender, height, and weight (Table 1).

Pain Reduction

At baseline, the GCSB-5 group had statistically significant higher NRS-11 scores for back pain compared to the placebo group (Table 2). Mean changes in NRS-11 scores for back pain from baseline to each post treatment commencement follow-up visit are shown in Table 2. The GCSB-5 group demonstrated greater statistically significant reductions in back pain NRS-11 scores at the 4-, 8-, and 16-week post treatment commencement follow-ups compared to the placebo group. For leg pain, baseline NRS-11 scores were not statistically significantly different between the 2 groups (Table 3). However, the GCSB-5 group had greater statistically significant reductions in leg pain NRS-11 scores at the 4-, 8-, 12-, and 16-week post treatment commencement follow-ups. Nevertheless, despite these differences in pain reduction, absolute NRS-11 scores for back and leg pain at all post treatment commencement follow-up time points were not significantly different statistically between the groups (Table 3).

Table 1. *Study patient baseline characteristics and adverse events.*

Variables	Placebo (n = 19)	GCSB-5 (n = 22)	*P* Value
Gender (men/women), n	13/6	12/10	0.364
Age (yrs), mean (SD)	44 (9.4)	40.55 (11.84)	0.313
Weight (kg), mean (SD)	62.61 (11.02)	66.64 (18.79)	0.401
Height (cm), mean (SD)	163.32 (5.56)	166.75 (9.06)	0.146

Functional Improvement and Quality of Life

Baseline ODI scores showed no statistically significant difference between the groups (Table 4). While changes in ODI scores at the 4-, 8-, and 12-week post treatment commencement follow-ups were not statistically significant, the GCSB-5 group exhibited a statistically significant greater reduction in ODI scores at post treatment commencement 16 weeks compared to the placebo group (Table 4).

Baseline SF-36 Physical Component Scores and Mental Component Scores were comparable between the 2 groups (Table 5). Although the GCSB-5 group showed a greater increase in the SF-36 Mental Component Score at the post treatment commencement 12-week follow-up, this difference was not observed at post treatment commencement weeks 4, 8, or 16. No statistically significant differences in Physical Component Score changes were observed in the SF-36 Physical Component Score between the groups at any of the post treatment commencement follow-ups.

Imaging Outcomes

Baseline Pfirrmann grades did not significantly differ statistically between groups, and no statistically significant differences were observed at the post treatment commencement 16-week follow-up (Table 6). Similarly, changes in anterior and posterior disc heights over time did not statistically differ between the 2 groups.

Table 2. *Comparison of Numeric Rating Scale scores for back pain between the GCSB-5 and placebo groups.*

Variables	Placebo (n = 19)	GCSB-5 (n = 22)	*P* Value
Baseline	5.58 (1.43)	6.86 (1.25)	0.002*
PTC 4 wks	4.00 (2.11)	3.96 (1.59)	0.915
PTC 8 wks	3.74 (1.88)	3.64 (1.84)	0.720
PTC 12 wks	3.10 (1.79)	3.23 (1.93)	0.863
PTC 16 wks	3.53 (2.12)	2.96 (1.50)	0.329
Δ PTC 4 wks (PTC 4 wks-baseline)	-1.58 (1.54)	-2.91 (1.57)	0.014*
Δ PTC 8 wks (PTC 8 wks-baseline)	-1.84 (1.26)	-3.23 (1.57)	0.005*
Δ PTC 12 wks (PTC 12 wks-baseline)	-2.47 (1.61)	-3.64 (1.94)	0.082
Δ PTC 16 wks (PTC 16 wks-baseline)	-2.05 (1.27)	-3.91 (1.54)	< 0.001*

PTC, post treatment commencement. Values are presented as mean (SD). *$P < 0.05$ is statistically significant.

Table 3. *Comparison of Numeric Rating Scale scores for leg pain between the GCSB-5 and placebo groups.*

Variables	Placebo (n = 19)	GCSB-5 (n = 22)	*P* Value
Baseline	3.26 (2.33)	5.55 (2.50)	0.088
PTC 4 wks	2.84 (2.12)	3.05 (1.86)	0.800
PTC 8 wks	2.21 (2.07)	3.05 (2.54)	0.427
PTC 12 wks	2.00 (2.03)	2.73 (2.62)	0.431
PTC 16 wks	1.53 (1.95)	2.55 (2.70)	0.152
Δ PTC 4 wks (PTC 4 wks-baseline)	-0.42 (1.61)	-2.50 (2.32)	0.020*
Δ PTC 8 wks (PTC 8 wks-baseline)	-1.05 (1.54)	-2.50 (2.28)	0.017*
Δ PTC 12 wks (PTC 12 wks-baseline)	-1.26 (1.94)	-2.82 (2.34)	0.028*
Δ PTC 16 wks (PTC 16 wks-baseline)	-1.74 (2.00)	-3.00 (2.00)	0.049*

PTC, post treatment commencement. Values are presented as mean (SD). *$P < 0.05$ is statistically significant.

Table 4. *Comparison of Oswestry Disability Index values between the GCSB-5 and placebo groups.*

Variables	Placebo (n = 19)	GCSB-5 (n = 22)	*P* Value
Baseline	29.05 (9.25)	34.09 (13.87)	0.249
PTC 4 wks	23.26 (9.40)	26.59 (11.24)	0.265
PTC 8 wks	20.84 (6.99)	24.91 (12.04)	0.455
PTC 12 wks	19.74 (9.38)	22.64 (11.70)	0.564
PTC 16 wks	21.90 (8.88)	18.77 (11.28)	0.260
Δ PTC 4 wks (PTC 4 wks-baseline)	-5.79 (7.15)	-7.50 (8.79)	0.431
Δ PTC 8 wks (PTC 8 wks-baseline)	-8.21 (8.37)	-9.18 (11.16)	0.511
Δ PTC 12 wks (PTC 12 wks-baseline)	-9.32 (11.36)	-11.46 (13.37)	0.927
Δ PTC 16 wks (PTC 16 wks-baseline)	-7.16 (9.89)	-15.32 (12.19)	0.031*

PTC, post treatment commencement. Values are presented as mean (SD). *$P < 0.05$ is statistically significant.

Rescue Medication Use

The overall use of rescue medications was low and did not statistically differ significantly between the 2 groups (Table 7). Specifically, acetaminophen was used by 5 patients in the GCSB-5 group and 4 participants in the placebo group. Oxycodone/naloxone was used by one patient in the GCSB-5 group and one patient in the placebo group. This suggests that the need for additional analgesics was low and comparable between the groups.

Table 5. *Comparison of Short Form-36 scores between the GCSB-5 and placebo groups over time.*

Variables	Placebo (n = 19)	GCSB-5 (n = 22)	*P* Value
Baseline PCS	47.97 (15.20)	54.55 (15.36)	0.170
Baseline MCS	54.26±16.83	62.18 (18.50)	0.182
PTC 4 wks PCS	59.58 (11.98)	57.00 (12.72)	0.301
PTC 4 wks MCS	64.84 (11.28)	64.05 (16.12)	0.763
PTC 8 wks PCS	59.58 (15.25)	58.18 (16.66)	0.647
PTC 8 wks MCS	64.37 (12.01)	62.86 (17.05)	0.505
PTC 12 wks PCS	66.32 (12.66)	62.96 (17.45)	0.464
PTC 12 wks MCS	68.84 (11.72)	64.77 (17.93)	0.388
PTC 4 wks PCS 16 weeks-PCS	61.74 (15.87)	64.18 (21.39)	0.647
PTC 16 wks MCS	67.68 (13.54)	67.14 (17.74)	0.886
Δ PTC 4 wks (PTC 4 wks-baseline) PCS	11.79 (16.77)	2.46 (10.83)	0.092
Δ PTC 4 wks (PTC 4 wks-baseline) MCS	10.58 (17.89)	1.84 (10.83)	0.123
Δ PTC 8 wks (PTC 8 wks-baseline) PCS	11.79 (16.44)	3.64 (18.00)	0.250
Δ PTC 8 wks (PTC 8 wks-baseline) MCS	10.11 (18.80)	0.68 (15.34)	0.099
Δ PTC 12 wks (PTC 12 wks-baseline) PCS	18.53 (8.41)	8.41 (16.57)	0.051
Δ PTC 12 wks (PTC 12 wks-baseline) MCS	14.58 (15.74)	2.60 (15.34)	0.017*
Δ PTC 16 wks (PTC 16 wks-baseline) PCS	13.95 (17.11)	9.64 (20.40)	0.628
Δ PTC 16 wks (PTC 16 wks-baseline) MCS	13.42 (17.76)	4.96 (16.99)	0.087

PCS, physical component score; MCS, mental component score; PTC, post treatment commencement. Values are presented as mean (SD). *$P < 0.05$ is statistically significant.

Safety and Adverse Events

Adverse events in both groups are summarized in Table 7. No statistically significant differences were found, indicating comparable safety profiles between the 2 groups.

Discussion

Our prospective, multicenter, double-blinded, randomized, placebo-controlled, clinical trial aimed to evaluate the efficacy and safety of GCSB-5 in patients with LDH. GCSB-5 and placebo tablets were administered over 12 weeks, with a follow-up period of 16 weeks. Although no structural improvements were observed following GCSB-5 administration, our study revealed that patients in the GCSB-5 group experienced greater reductions in back and leg pain compared to

the placebo group at most follow-up time points. Additionally, the GCSB-5 group's improvements in ODI scores at post treatment commencement 16 weeks and the SF-36 Mental Component Scores in at post treatment commencement 12 weeks, suggest that GCSB-5 may enhance daily functional capacity and mental well-being, making GCSB-5 a promising therapeutic option for patients with LDH.

Interestingly, although LDH is typically characterized by predominant radicular pain in the leg rather than back pain, our patients tended to report a higher degree of back pain throughout the study period. This discrepancy may be attributed to the characteristics of our study population; many of them had relatively small herniated disc sizes without significant nerve root compression. Consequently, back pain appeared to be more prominent than radiating leg pain in our study.

Previous studies have investigated the effects of GCSB-5 in patients with osteoarthritis in the knee and wrist (9,10). Park, et al (10) compared GCSB-5 to celecoxib in patients with knee osteoarthritis and demonstrated that GCSB-5 was comparable to celecoxib in terms of pain relief and functional improvement. In another trial involving hand osteoarthritis, GCSB-5 statistically reduced pain significantly and improved joint function compared to a placebo. Our study extends these findings, suggesting that GCSB-5 may also benefit patients with LDH (9).

The safety profile of GCSB-5 was comparable to the placebo group in our study, with no serious adverse events reported. Mild adverse events, such as drowsiness and transient elevations in alanine aminotransferase/aspartate aminotransferase levels, were manageable and did not necessitate treatment discontinuation. Similarly, Park, et al (10) reported that the adverse event profile of GCSB-5 was comparable to that of the placebo, indicating a favorable safety profile for the herbal formulation. Previous studies have also indicated that GCSB-5 is associated with good gastrointestinal safety since no cases of perforation, obstruction, bleeding, or ulcers have been reported (8,9,16). This favorable safety profile positions GCSB-5 as a viable alternative to conventional nonsteroidal anti-inflammatory drugs, which are known to carry significant gastrointestinal and cardiovascular risks.

Regarding its mechanism of action, prior studies have shown that GCSB-5 not only exerts anti-inflammatory effects, but also reduces neuronal activity and attenuates pain sensitization (11,12,17). Specifi-

Table 6. *Magnetic resonance imaging findings: Comparison of the Pfirrmann Grade, and disc height between the GCSB-5 and placebo groups.*

Variables	Placebo (n = 19)	GCSB-5 (n = 22)	*P* Value
Pfirrmann Grade			
Baseline, mean (SD)	5.16 (1.26)	4.86 (1.32)	0.976
Grade III, n (%)	2 (10.53%)	4 (18.18%)	
Grade IV, n (%)	4 (21.05%)	5 (22.73%)	
Grade V, n (%)	5 (26.32%)	6 (27.27%)	
Grade VI, n (%)	5 (26.32%)	4 (18.18%)	
Grade VII, n (%)	3 (15.79%)	3 (13.64%)	
Final Visit, mean (SD)	4.63 (1.06)	4.36 (1.18)	0.65
Grade III, n (%)	2 (10.53%)	5 (22.73%)	
Grade IV, n (%)	8 (42.11%)	9 (40.91%)	
Grade V, n (%)	5 (26.32%)	5 (22.73%)	
Grade VI, n (%)	3 (15.79%)	1 (4.55%)	
Grade VII, n (%)	1 (5.26%)	2 (9.09%)	
Anterior disc height, mean (SD)			
Visit One	10.72 (2.89)	10.86 (2.25)	0.926
Visit 6	10.99 (2.93)	11.40 (2.32)	0.775
Δ Baseline to Final Visit	0.27 (0.89)	0.55 (0.98)	0.324
Posterior disc height, mean (SD)			
Visit One	7.73 (1.29)	7.63 (1.27)	0.836
Visit 6	7.43 (1.66)	7.40 (1.10)	0.651
Δ Baseline to Final Visit	-0.30 (1.11)	-0.23 (0.84)	0.823

Table 7. *Comparison of rescue medication use and adverse events.*

Variables	Placebo (n = 19)	GCSB-5 (n = 22)	*P* Value
Rescue medications, n (%)			
Acetaminophen	4 (21.05%)	5 (22.73%)	1.000
Oxycodone/naloxone	1 (5.26%)	1 (4.55%)	1.000
Adverse events, n (%)			
Drowsiness	0 (0)	4 (18.18%)	0.111
Transient mild ALT/AST elevation	0 (0)	2 (9.09%)	0.490
GI complication	2 (10.53%)	0 (0)	0.209
URI	2 (10.53%)	0 (0)	0.209
Skin rash	2 (10.53%)	2 (9.09%)	1.000
Headache	0 (0)	2 (9.09%)	0.490
Cold	3 (15.79%)	2 (9.09%)	0.649
Eye	0 (0)	3 (13.64%)	0.235
Dizziness	0 (0)	1 (4.55%)	1.000

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GI, gastrointestinal; URI, upper respiratory infection.

cally, GCSB-5 has been shown to inhibit the activity of neuropeptides, nociceptors, and neurotrophic factors (13,14,18). Additionally, previous studies have demonstrated that Eucommiae cortex and Acanthopanacis cortex possess significant antioxidant activity (19, 20). Additionally, Additionally, Eucommiae cortex has been shown to exert anti-inflammatory effects by suppressing COX-2 (21). One of its active compounds has been shown to downregulate pro-inflammatory cytokines such as interleukin-1β and tumor necrosis factor-α (22,23). Furthermore, Acanthopanacis cortex exerts anti-inflammatory effects by modulating nuclear factor-κB signaling and inhibition of nitric oxide synthase (24,25). It also contains Ledebouriellae radix, Achyranthis radix, Cibotii rhizoma, and Glycini semen, which are known to have analgesic properties (26).

Moreover, GCSB-5 appears to protect against cartilage degradation in osteoarthritis by inhibiting matrix metalloproteinases (27). We believe that the mechanisms described above contribute to pain relief for patients with LDH, and can improve patients' function and quality of life.

Our study's strengths include its double-blinded, placebo-controlled design, which minimized bias. We also used validated tools, such as the NRS-11, ODI, and SF-36, ensuring robust evaluation of clinical outcomes. Although GCSB-5 did not demonstrate structural benefits, pre- and posttreatment MRIs were conducted to assess any anatomical changes.

Limitations

Our study has some limitations. First, the short study duration limits the generalizability of the findings. Second, this study is limited by its small sample size, with only 46 patients randomized and 41 completing the trial. This reduces the statistical power and limits the generalizability of the results. Third, NRS-11 scores were statistically significantly higher at baseline in the GCSB-5 group compared to placebo, which may have introduced bias and affected the results. Fourth, although change-from-baseline improvements were statistically significant, absolute NRS-11 and ODI scores at follow-up did not differ between groups, raising concerns about the clinical significance of the findings. Fifth, rescue medication use may have affected the outcomes. Lastly, the absence of biochemical markers precluded analyzing the specific anti-inflammatory mechanisms of GCSB-5. Future studies that can address these limitations are warranted.

Conclusions

Our study suggests that GCSB-5 may reduce pain in patients with LDH, with potential improvement in functional ability and mental well-being. However, given the short duration, small sample size, and modest outcomes, these findings should be considered preliminary. Further studies complementing the limitations of our study are needed to further evaluate the effectiveness of GCSB-5 as a therapeutic option for managing LDH.

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