

A Berberine-containing combination preparation and ultrasound-derived fat fraction in hepatic steatosis: a single-center observational case series

6 Bernhard Sikora¹, Babak Malekian^{2*} , Agnieszka
7 Magg³, Nikon Moghadasian⁴, Mohammed
8 Moghadasian⁵, Oliver Lammel⁶, Afsaneh Gachter⁷,
9 Babak Bahadori⁸



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10 ABSTRACT

Background: Hepatic steatosis is the most common chronic liver disease, but pharmacologic options remain limited. Berberine reduces hepatic fat in randomized trials, but has very low oral bioavailability and has been studied almost exclusively as high-dose (1.0-1.5 g/day) capsules.

Case Presentation: We report a single-center, retrospective, uncontrolled before–after case series of 25 adults with ultrasound-defined hepatic steatosis who used a liquid berberine-containing combination preparation during routine care, without a prescribed lifestyle intervention or control group. Twenty patients (16 men; mean age 57 years) had paired ultrasound-derived fat fraction (UDFF) measurements and were included in the complete-case analysis; five lacked follow-up measurements. After a median of 7 weeks, UDFF decreased from $18.2\% \pm 6.3\%$ to $11.2\% \pm 4.8\%$ among complete cases (mean change -7.1 percentage points; 95% CI -9.1 to -5.0 ; $p < 0.001$). All 20 complete cases had a lower follow-up value, and 12 (60%) had a $\geq 30\%$ relative reduction. In a conservative sensitivity analysis assigning zero change to the five patients without follow-up, the mean change was -5.6 percentage points and 12 of 25 (48%) met the $\geq 30\%$ threshold. No adverse events were documented in the available routine-care records.

Conclusion: These uncontrolled observations cannot establish efficacy or identify which component, if any, contributed to the observed change. The findings are susceptible to attrition bias, regression to the mean, unmeasured clinical or lifestyle changes, observation effects, and unblinded measurement. They should be considered hypothesis-generating and require confirmation in an independent randomized controlled trial.

27 **Keywords:** Hepatic steatosis, berberine, Berberis, ultrasound-derived fat fraction, case series.

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29 Correspondence to: Babak Malekian

*Department of Ecosystem Management, Climate and Biodiversity,
the University of Natural Resources and Life Sciences (BOKU), Vienna,
Austria.

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33 Email: babak.malekian@boku.ac.at

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Full list of author information is available at the end of the article.

38 Background

Hepatic steatosis, fat accumulation in the liver, occurring with or without a confirmed cardiometabolic risk factor, is among the most common findings on abdominal ultrasound and the hallmark feature of metabolic dysfunction-associated steatotic liver disease (MASLD), the metabolism-based term adopted by international consensus in 2023 for steatosis occurring alongside cardiometabolic risk factors [1]. The patients in this series had documented metabolic syndrome and ultrasonographic hepatic steatosis. We nevertheless use the broader term hepatic steatosis because the retrospective records did not contain sufficiently complete individual cardiometabolic data to

verify all contemporary MASLD criteria systematically; the disease burden context (progression to steatohepatitis, fibrosis, cirrhosis; epidemiologic links to type 2 diabetes [2]) nonetheless derives chiefly from the MASLD literature; whether this series' patients would all meet MASLD criteria was not verified. Until the recent approvals of the thyroid-hormone-receptor- β agonist resmetirom [3] and, more recently, the GLP-1 receptor agonist semaglutide for steatohepatitis with moderate-to-advanced fibrosis, management rested almost entirely on weight loss and lifestyle modification, which are hard to sustain. There is therefore continued interest in accessible, low-risk interventions that reduce hepatic fat.

64	Berberine, an isoquinoline alkaloid found in <i>Berberis</i>	117
65	and <i>Coptis</i> species, is among the most studied natural	118
66	compounds in this setting. In a three-arm randomized	119
67	trial, berberine 1.5 g/day added to lifestyle intervention	120
68	reduced hepatic fat content by 52.7% over 16 weeks,	
69	significantly more than lifestyle alone (-36.4%) [4], and	
70	subsequent randomized trials and meta-analyses have	
71	reported favorable, though not uniform, effects on liver	
72	fat and metabolic parameters [5–7,14]. A central lim-	
73	itation of berberine is its very low oral bioavailability	
74	(approximately 0.7% in rats [8], with steady-state plasma	
75	concentrations of only a few nanograms per milliliter in	
76	humans at 1.5 g/day [4,9]), owing to poor absorption,	
77	<i>P</i> -glycoprotein-mediated efflux, and extensive first-pass	
78	metabolism. Almost all clinical studies have used high-	
79	dose (1.0–1.5 g/day) capsules or tablets.	
80	Whether the galenic form of berberine influences its	
81	effect on hepatic steatosis has, to our knowledge, not	
82	been described. Separately, the assessment of liver fat	
83	is changing: ultrasound-derived fat fraction (UDFF), an	
84	AI-assisted quantitative ultrasound technique, correlates	
85	closely with magnetic-resonance proton-density fat frac-	
86	tion and histology and is reproducible across operators	
87	[10,11], making longitudinal, point-of-care quantification	
88	feasible in routine practice.	
89	We describe an observational case series in which	
90	hepatic fat, measured by UDFF, was tracked before and	
91	after use of a low-dose liquid berberine-containing com-	
92	bination preparation in consecutive patients at a single	
93	Austrian practice. The series is explicitly hypothesis-gen-	
94	erating and is not intended to establish efficacy.	
95	Methods	
96	Setting and patients	
97	This was a retrospective, uncontrolled before–after obser-	
98	vatinal study, reported in accordance with the STROBE	
99	statement for observational studies [12]. Between	
100	November 2025 and May 2026, 25 consecutive adults	
101	attending a single general practice in Austria who had	
102	ultrasonographic hepatic steatosis elected to use the liq-	
103	uid berberine-containing combination preparation and	
104	underwent baseline UDFF measurement. Twenty patients	
105	had an available follow-up UDFF measurement and were	
106	included in the complete-case analysis. Five patients had	
107	no follow-up UDFF measurement available by the data	
108	cutoff and were therefore not included in the paired anal-	
109	ysis. Three had undergone baseline examination late in	
110	the observation period and their follow-up measurements	
111	were not yet available at the data cutoff, while two did	
112	not return for their scheduled follow-up examination. No	
113	follow-up outcome existed for any of these five patients;	
114	therefore, none was omitted on the basis of a known	
115	favorable or unfavorable outcome. Their age, sex, base-	
116	line UDFF, and baseline examination dates are reported in	
	Supplementary Table S1. There was no randomization, no	117
	control group, and no prescribed dietary or physical-ac-	118
	tivity program. One patient (P06) became non-adherent	119
	during follow-up and was analyzed as observed.	120
	Available clinical characteristics	121
	The patients had documented metabolic syndrome and	122
	ultrasonographic hepatic steatosis. No dietary or phys-	123
	ical-activity intervention was prescribed. The available	124
	clinical histories did not indicate relevant alcohol con-	125
	sumption, known cardiovascular disease, or active malig-	126
	nancy. Individual BMI and weight change, diabetes status,	127
	concomitant medications, complete lipid profiles, liver	128
	enzymes, and other comorbidities were not systematically	129
	available for the entire cohort. Available routine biochem-	130
	ical measurements from a subset are reported descrip-	131
	tively in Table 3.	132
	Intervention	133
	The berberine-containing combination preparation	134
	(Berberstin, manufactured by BerBerSan, Austria) is	135
	a liquid food supplement and not a licensed medicinal	136
	product. According to the manufacturer’s specifications,	137
	each 15-ml dose contains 100 mg of berberine hydrochlo-	138
	ride (stated purity $\geq 97\%$) derived from <i>Berberis aristata</i> ,	139
	together with cold-pressed <i>Berberis vulgaris</i> fruit extract.	140
	The preparation’s composition was not independently	141
	assayed. Patients took one dose before the first meal and	142
	one after the last meal of the day, corresponding to a manu-	143
	facturer-specified total of 200 mg/day of berberine hydro-	144
	chloride, and briefly held each dose in the mouth before	145
	swallowing. No pharmacokinetic measurements were per-	146
	formed, and there is no established evidence of clinically	147
	relevant oromucosal or sublingual absorption of berber-	148
	ine in humans. The preparation is therefore described as	149
	a swallowed liquid oral combination preparation rather	150
	than a sublingual formulation. The brief oral contact is	151
	reported only as part of the administration procedure and	152
	is not proposed as a mechanism of action. Because the	153
	preparation contained both berberine hydrochloride and	154
	<i>B. vulgaris</i> fruit extract, any observed change cannot be	155
	attributed specifically to berberine or to either individual	156
	component.	157
	UDFF measurement	158
	Hepatic fat was quantified by ultrasound-derived fat frac-	159
	tion using a Siemens ACUSON Sequoia system with the	160
	AI-assisted UDFF package. Measurements were obtained	161
	from the right hepatic lobe, and the median of five inter-	162
	costal acquisitions was recorded at each visit. All exam-	163
	inations were performed by the same operator, who had	164
	received training from Siemens Healthineers, using the	165
	same ultrasound system and the standardized measure-	166
	ment procedure recommended by the manufacturer. The	167
	use of the same operator, system, anatomical approach, and	168

acquisition procedure was intended to reduce inter-operator and technical variability. The operator was aware that the patients were using the berberine-containing combination preparation; therefore, the follow-up examinations were not blinded to exposure. The retrospective records did not document whether the baseline UDFF value was concealed from the operator during the follow-up examination, and access to or recollection of the baseline result cannot be excluded. Study-specific intra-operator repeatability was not formally assessed. Detailed information regarding fasting duration and all technical acquisition settings was not systematically documented in the retrospective dataset; consequently, identical fasting and technical conditions at both visits cannot be independently verified. Steatosis grade was assigned using MRI-PDFF-derived fat-fraction thresholds applied for exploratory descriptive purposes.

Follow-up

Follow-up UDFF was obtained at a routine return visit. In this real-world setting, the interval was not fixed: among patients with reliable dates, it was a median of 7 weeks (range 4–18 weeks). Three patients underwent a further, later scan. Individual follow-up intervals were not available for all patients in the retrospective dataset beyond the recorded median and range; therefore, a patient-level analysis of the association between treatment duration and UDFF change could not be performed. This is acknowledged as a limitation.

Outcomes and statistics

The primary descriptive outcome was the within-patient change in UDFF. Because the within-patient differences departed from normality on the Shapiro–Wilk test, paired baseline and follow-up values were compared primarily with the Wilcoxon signed-rank test, with the paired *t*-test reported for concordance; the within-subject effect size (Cohen’s *d*) and the 95% confidence interval of the mean change were calculated. Responder proportions were summarized at absolute (≥ 5 percentage-point) and relative ($\geq 30\%$) thresholds as an exploratory analysis; no dated, pre-registered analysis plan exists for this threshold. Analyses were performed in Python (SciPy) and independently reproduced in a spreadsheet. Available paired routine laboratory values in a subset are reported descriptively. The primary analysis was a complete-case analysis restricted to the 20 patients with both baseline and follow-up UDFF measurements. Baseline characteristics of the five patients without follow-up were summarized descriptively. Because their follow-up outcomes were unavailable, the missing values could not be assumed to be missing completely at random. A conservative non-responder sensitivity analysis was therefore performed in which the five patients without follow-up were assigned zero change from baseline, equivalent to

baseline observation carried forward. This was not considered a true worst-case analysis because UDFF could theoretically have increased among the patients without follow-up.

Ethics and consent

This work is a retrospective, de-identified documentation of the voluntary use of a commercially available food supplement during routine clinical care. The preparation was not assigned under a research protocol, and no prospective intervention was conducted. On this basis, the authors considered that the work was not a clinical trial of a medicinal product under Regulation (EU) No 536/2014 and the Austrian Medicines Act, not a clinical investigation of a medical device under Regulation (EU) 2017/745, and not the prospective application of a new medical method within the meaning of § 8c KAKuG. The authors therefore considered that the cited provisions requiring ethics-committee involvement did not apply. No formal ethics-committee exemption or determination was obtained. All patients provided written informed consent for the use and publication of their anonymized clinical data and images.

Results

Cohort

The complete-case cohort comprised 20 patients (16 men and 4 women) with a mean age of 56.8 ± 13.5 years (range 29–72). Their mean baseline UDFF was $18.2\% \pm 6.3\%$ (median 17.5%; range 8%–29%), corresponding to seven patients in the S1 band, 10 in the S2 band, and 3 in the S3 band (Table 1). These MRI-PDFF-derived bands were used for exploratory description and have not been independently validated for UDFF. All 20 patients included in the complete-case analysis had an available follow-up UDFF measurement. One patient (P06) became non-adherent during follow-up and was analyzed as observed.

Participants without follow-up

Five of the 25 patients with baseline UDFF measurements had no follow-up measurement available by the data cut-off and were not included in the paired complete-case analysis. These five patients comprised two men and three women and had a mean age of 60.6 years. Their mean baseline UDFF was 22.0% (median 21%; range 15%–27%), compared with 18.2% (median 17.5%; range 8%–29%) among the 20 complete cases. Thus, the patients without follow-up had a numerically higher mean baseline UDFF, although their subsequent UDFF trajectories are unknown. Their individual sex, age, baseline UDFF, and baseline examination dates are provided in Supplementary Table S1.

Table 1. Per-patient characteristics and ultrasound-derived fat fraction (UDFF) at baseline and follow-up (20 patients). P06 became non-adherent during follow-up (on-treatment value shown). pp, percentage points; FU, follow-up. Grades: S0 < 5%, S1 5%–14.9%, S2 15%–24.9%, S3 ≥ 25%.

ID	SEX	AGE	BASELINE UDFF (%)	FOLLOW-UP UDFF (%)	ABSOLUTE Δ (PP)	RELATIVE Δ (%)	GRADE (BASE→FU)
P01	M	68	26	14	–12	–46%	S3→S1
P02	M	49	11	9	–2	–18%	S1→S1
P03	F	71	11	8	–3	–27%	S1→S1
P04	M	29	9	5	–4	–44%	S1→S1
P05	M	69	18	15	–3	–17%	S2→S2
P06	M	53	13	7	–6	–46%	S1→S1
P07	M	72	24	8	–16	–67%	S2→S1
P08	M	72	23	19	–4	–17%	S2→S2
P09	F	67	13	4	–9	–69%	S1→S0
P10	M	55	22	14	–8	–36%	S2→S1
P11	M	33	22	16	–6	–27%	S2→S2
P12	M	35	28	12	–16	–57%	S3→S1
P13	M	63	14	11	–3	–21%	S1→S1
P14	M	43	8	5	–3	–37%	S1→S1
P15	F	58	16	8	–8	–50%	S2→S1
P16	M	65	16	10	–6	–37%	S2→S1
P17	F	67	23	17	–6	–26%	S2→S2
P18	M	48	17	6	–11	–65%	S2→S1
P19	M	63	21	18	–3	–14%	S2→S2
P20	M	56	29	17	–12	–41%	S3→S2
Mean		56.8	18.2	11.2	–7.1	–38.3%	

Primary change

Representative paired ultrasound images illustrating the changes in UDFF at baseline and follow-up are presented in Figure 3. Among the 20 patients with paired measurements included in the complete-case analysis, follow-up UDFF was $11.2\% \pm 4.8\%$ (median 10.5%). The mean within-patient change was -7.1 percentage points (95% CI -9.1 to -5.0). Because the within-patient differences departed from normality (Shapiro–Wilk $p = 0.02$), the Wilcoxon signed-rank test was used as the primary analysis ($p < 0.001$); the paired t-test produced a concordant result ($p < 0.0001$). The within-patient effect size was Cohen’s $d_z = -1.6$, and the mean relative reduction was 38.3% (median 37.5%) (Figure 1). These estimates apply only to the 20 patients with available paired measurements.

Exploratory response summaries

Among the 20 complete cases, all had a lower follow-up UDFF value than at baseline. Twelve of 20 (60%) had a ≥30% relative reduction, 12 of 20 (60%) had a ≥5-percentage-point absolute reduction, and 5 of 20 (25%) had a ≥50% relative reduction (Figure 2). Nine of 20 (45%) crossed at least one exploratory MRI-PDFF-derived steatosis band, none crossed to a higher band, and one patient reached a value below 5%. These findings describe only the observed complete cases and should not be interpreted as a 100% treatment-response rate.

Attrition sensitivity analysis

In a conservative analysis assigning zero change to all five patients without follow-up, the mean change across the full baseline cohort of 25 patients was -5.6 percentage points. Twenty of 25 patients (80%) had an observed reduction, and 12 of 25 (48%) met the exploratory ≥30% relative-reduction threshold. The five patients without follow-up were classified as non-responders in this analysis. Although the estimates were attenuated compared with the complete-case results, this analysis cannot establish the actual outcomes of the five patients without follow-up or eliminate residual attrition bias.

Baseline dependence

Patients with higher baseline UDFF tended to show larger absolute reductions (Pearson $r = -0.65$) (Supplementary Figure S1). Because baseline values appear in both terms of this comparison, the correlation is inflated by mathematical coupling and regression to the mean and should not be read as a treatment-by-severity interaction; baseline and follow-up values remained positively correlated ($r = 0.73$).

Later course

Three patients underwent a further scan after the on-treatment measurement. Two showed partial rebound of liver fat, and the patient who became non-adherent (P06) rose

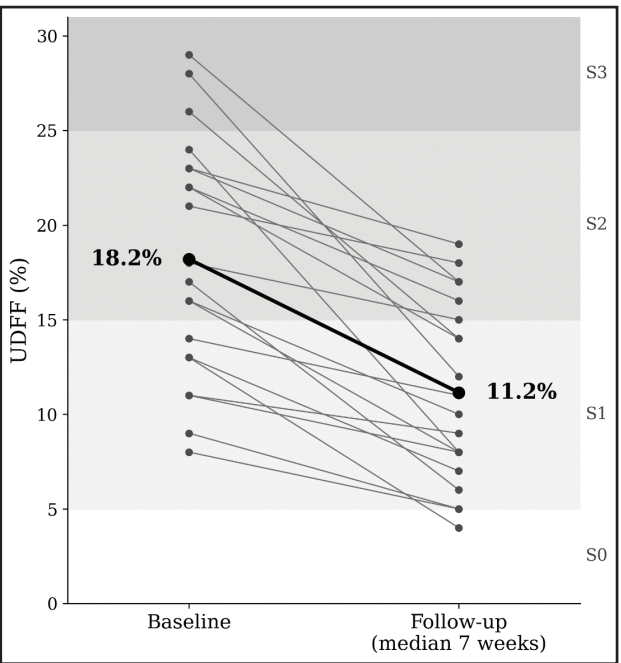


Figure 1. Paired hepatic ultrasound-derived fat fraction (UDFF) at baseline and follow-up after use of the combination preparation among the 20 complete cases. Individual patient trajectories are shown by gray lines and circles, and the bold black line indicates the cohort mean. The shaded horizontal bands represent MRI-PDFF-derived thresholds (S0 < 5%, S1 5–14.9%, S2 15–24.9%, and S3 ≥ 25%) applied for exploratory descriptive purposes only. These thresholds have not been independently validated as UDFF steatosis grades.

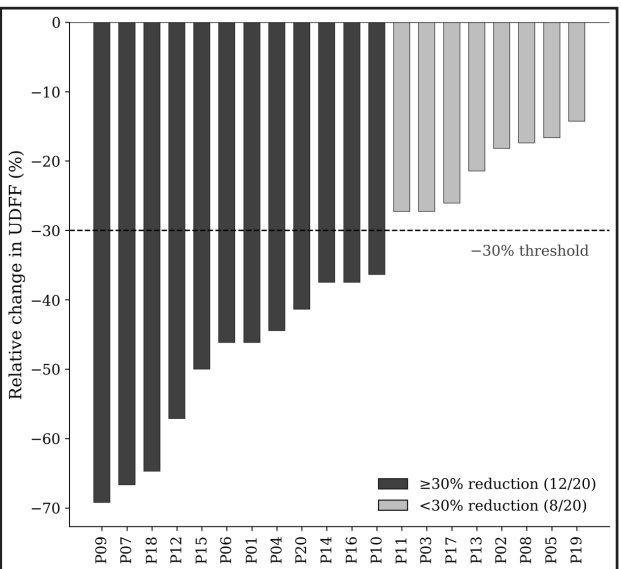


Figure 2. Per-patient relative change in hepatic ultrasound-derived fat fraction (UDFF) (n = 20). Bars are ordered by magnitude of relative change. Dark bars indicate patients who reached the exploratory ≥ 30% relative reduction threshold; light bars indicate those who did not. The dashed line marks the -30% threshold.

back toward baseline (13% → 7% → 11%). These within-patient observations are anecdotal and compatible with several explanations, including an adherence-dependent effect, regression to the mean, or unrelated fluctuation; no causal inference can be drawn, and durability of

any effect could not be assessed in this series. Because P06’s primary-analysis value (7%) was the last on-treatment measurement rather than the latest available one, we checked whether substituting the last-observed value (11%) changes the result: the cohort mean follow-up shifts from 11.2% to 11.35%, mean change from -7.1 to -6.9 percentage points, and the proportion with a ≥30% relative reduction went from 12/20 (60%) to 11/20 (55%), the result was materially unchanged.

Biochemistry (exploratory)

Paired routine laboratory values were available for 8 patients at non-standardized intervals. Median aminotransferases trended downward (AST 33→27 U/l, n = 5; ALT 45→38 U/l, n = 5), as did total cholesterol (227→213 mg/dl, n = 8); one patient with markedly elevated baseline transaminases improved substantially (AST 178→74, ALT 204→87 U/l). Changes in triglycerides and other markers were inconsistent and influenced by outliers. Given the small heterogeneous subset and irregular timing, these biochemical observations are descriptive only (Table 3).

Tolerability observations

Adverse events were not collected using a prospective standardized questionnaire or active surveillance procedure. No adverse events were documented in the available routine-care records. Some patients reported a bitter taste, which did not lead to documented discontinuation. These observations are insufficient to establish safety or estimate the frequency of adverse events.

Discussion

In this single-center observational series, mean UDFF decreased by 7.1 percentage points among 20 patients with paired measurements who used a berberine-containing combination preparation. All 20 complete cases had a lower follow-up value, and 45% crossed at least one exploratory MRI-PDFF-derived band. However, the directionally concordant finding must be interpreted in the context of complete-case analysis, lack of a control group, unblinded repeat measurement, regression to the mean, and incomplete confounder data. It cannot establish efficacy or be attributed to the preparation or any individual component.

Context

A descriptive comparison of the present case series with selected previous clinical studies of berberine is provided in Table 2. Controlled studies of berberine and berberine-derived formulations provide relevant background but are not directly comparable with the present observational series. Previous trials differed substantially in study design, formulation, dose, treatment duration, patient population, concomitant lifestyle intervention, and method of liver-fat assessment. Berberine at 1.5 g/day was investigated in

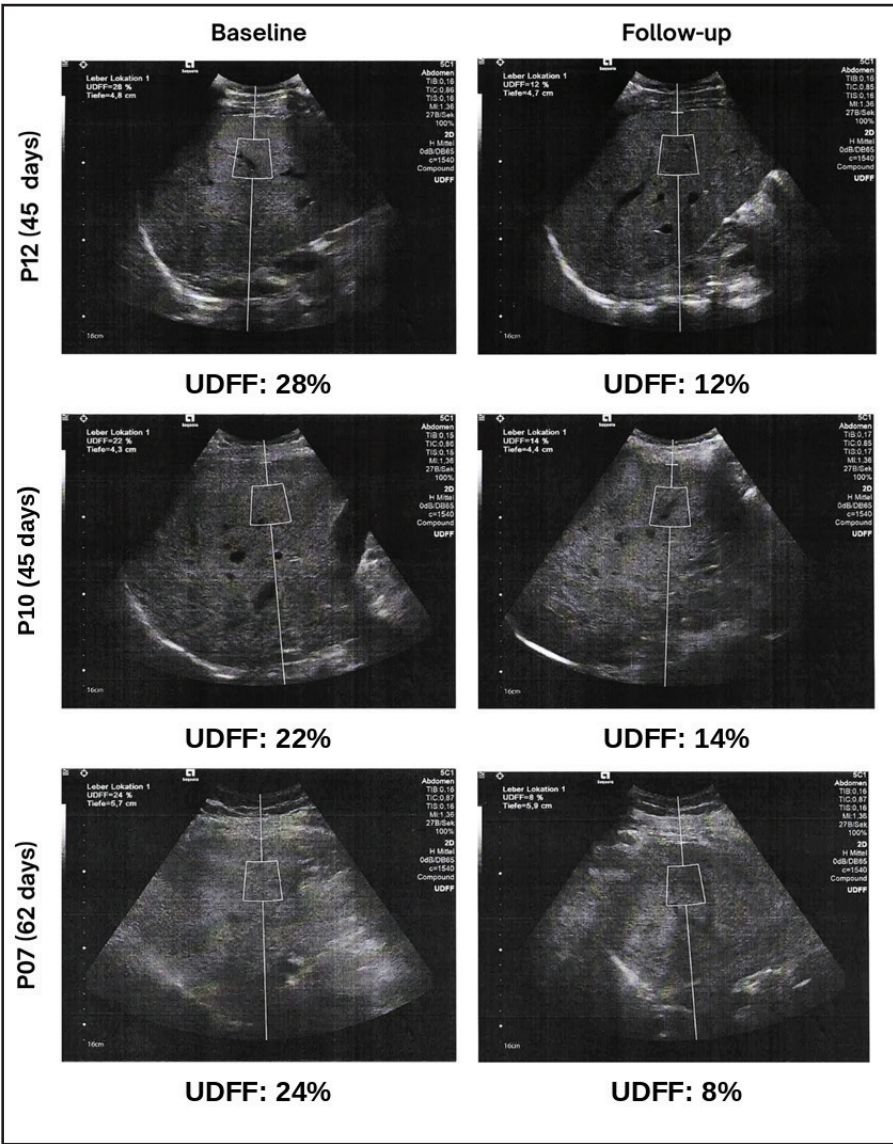


Figure 3. Representative paired ultrasound-derived fat fraction (UDFF) images at baseline and follow-up for three patients. Enlarged UDFF values are displayed below each panel to facilitate comparison and verification against the patient-level data in Table 1.

Table 2. This series in the context of selected berberine and reference studies in steatotic liver disease. Doses and durations differ markedly; comparisons are descriptive only and not adjusted. UDFF, ultrasound-derived fat fraction; MRI-PDFF, magnetic-resonance proton-density fat fraction; pp, percentage points.

STUDY (DESIGN)	N	PREPARATION, DOSE, AND FORMULATION	DURATION	IMAGING	LIVER-FAT CHANGE
This series (observational, uncontrolled)	20	Combination preparation containing a manufacturer-specified 200 mg/day berberine HCl plus Berberis vulgaris fruit extract; liquid oral formulation	~7 weeks (4–18)	UDFF	–7.1 pp; –38%; 100% reduced
Yan 2015 [4] (RCT, 3-arm, open-label)	184	1.5 g/day, capsule	16 weeks	MRS	–52.7% vs –36.4% lifestyle
Koperska 2024 [5] (RCT, placebo)	70	1.5 g/day, capsule	12 weeks	— (ALT/FLI)	↓ ALT (modest), total cholesterol
Harrison 2021 [13] (RCT, phase 2)	100	2 g/day, berberine ursodeoxycholate	18 weeks	MRI-PDFF	–4.8 vs –2.0 pp placebo
Nejati 2022 [6] (RCT)	50	6.25 g/day, decoction	6 weeks	— (enzymes/lipids)	No significant change (null)

UDFF, ultrasound-derived fat fraction; MRI-PDFF, magnetic resonance imaging proton density fat fraction; MRS, magnetic resonance spectroscopy; RCT, randomized controlled trial; ALT, alanine aminotransferase; FLI, Fatty Liver Index; pp, percentage points.

Table 3. Exploratory biochemistry subgroup (paired first vs last routine values), available for 8 patients at non-standardized intervals (not the UDFF timepoint); means are outlier-influenced, so medians are shown. Hypothesis-generating only; no inferential testing. AST/ALT/GGT in U/l; lipids in mg/dl.

MARKER (UNITS)	MEDIAN FIRST	MEDIAN LAST	N PAIRED	DIRECTION
AST (U/l)	33	27	5	↓ (4/5)
ALT (U/l)	45	38	5	↓ (3/5)
GGT (U/l)	58	45	8	mixed (4/8)
Triglycerides (mg/dl)	173	198	8	mixed
Total cholesterol (mg/dl)	227	213	8	↓ (4/8)

a 16-week trial that included lifestyle intervention [4], while a 2024 placebo-controlled trial evaluated its effects on hepatic and metabolic parameters over 12 weeks [5]. A phase 2 trial of berberine ursodeoxycholate reported a greater reduction in MRI-measured liver fat than placebo [13]. However, other randomized evidence has been null or inconsistent [6,7]. These findings cannot be used to infer comparable efficacy, dose equivalence, or enhanced bioavailability for the berberine-containing combination preparation evaluated in the present study. Its composition, dose, and formulation differ from those used in the controlled trials, and pharmacokinetics were not assessed.

Interpreting the formulation and dose

The present study cannot determine whether the observed UDFF change was related to berberine hydrochloride, *B. vulgaris* fruit extract, their combination, or factors unrelated to the preparation. The liquid vehicle and administration method differ from those used in previous capsule-based studies, but their influence on dissolution or intestinal absorption is unknown. No pharmacokinetic measurements were performed, and enhanced bioavailability is not claimed. Alternative explanations for the observed change include regression to the mean, unmeasured lifestyle or clinical changes, observation effects, and the absence of a control group. Although both berberine and constituents of the *B. vulgaris* fruit extract have biologically plausible metabolic effects, such plausibility cannot identify the responsible component or establish causality.

Strengths and limitations

The principal strength is the use of a validated, reproducible quantitative biomarker (UDFF) applied identically at both visits [10,11], which makes the within-patient changes more credible than echogenicity-based impressions. The limitations are substantial and constrain any inference. There was no control or placebo group and no randomization; No dietary or physical-activity intervention was prescribed, and body weight was documented as remaining clinically unchanged during follow-up. However, individual anthropometric values, spontaneous lifestyle changes, diabetes status, concomitant medications, complete lipid profiles, liver enzymes, and other relevant comorbidities

were not systematically available for the entire cohort. Residual confounding by these factors therefore cannot be excluded; the sample is modest, predominantly male, and from one practice, limiting generalizability including across populations, since UDFF results vary by ethnicity. Follow-up was short and its interval not standardized (4-18 weeks), so durability is unknown and could not be assessed in this series. Attrition is an additional limitation. Five of the 25 patients with baseline UDFF measurements had no follow-up value, and the primary analysis was therefore restricted to the 20 complete cases. The patients without follow-up had a numerically higher mean baseline UDFF than the analyzed cohort, but their subsequent UDFF trajectories are unknown. The complete-case estimate may be unbiased only under assumptions about the missing-data mechanism that cannot be verified. If follow-up attendance was associated with adherence, tolerability, perceived benefit, disease course, or other prognostic factors, the complete-case analysis could have overestimated or underestimated the change in the full baseline cohort. Although a conservative non-responder sensitivity analysis, in which the five patients without follow-up were assigned zero change from baseline, attenuated the estimated mean change from -7.1 to -5.6 percentage points, residual attrition bias cannot be excluded. UDFF, although accurate, is operator-dependent and not a histologic reference. Finally, several authors have a commercial interest in the product (declared above); although the analyses were independently verified and null and unfavorable findings are reported, this conflict warrants caution. For these reasons, the series is hypothesis-generating only. The steatosis-grade thresholds applied are conventional MRI-PDFF cutoffs and have not been independently validated for UDFF; grade-transition counts should be read as exploratory.

The directionally concordant decrease among all 20 complete cases is unusual for an uncontrolled routine-care series and requires particularly cautious interpretation. Although the same trained operator, ultrasound system, anatomical approach, manufacturer-recommended procedure, and median of five acquisitions were used at both visits, the operator knew that the patients were using the combination preparation. The examinations were therefore

not blinded to exposure. The retrospective records did not establish whether the baseline UDFF result was concealed during the follow-up examination, and access to or recollection of the baseline value cannot be excluded. Study-specific intra-operator repeatability was not formally assessed, and detailed fasting and technical conditions were not systematically documented. Consequently, expectation effects, operator-dependent variability, or differences in examination conditions may have contributed to the observed concordance.

Follow-up timing varied from 4 to 18 weeks. Because complete patient-level timing data were not available for analysis, we could not determine whether the magnitude of UDFF change was associated with follow-up duration.

Implications

The observed association provides a rationale for further controlled investigation of the complete combination preparation. A randomized, placebo-controlled study with standardized follow-up timing, blinded UDFF assessment, documented lifestyle and anthropometric data, adherence monitoring, and pharmacokinetic measurements would be required to distinguish any preparation-related effect from regression to the mean, measurement variability, and behavioral or clinical changes. Additional comparator groups would be necessary to determine whether any observed effect is related to berberine hydrochloride, the *B. vulgaris* fruit extract, or their combination.

Conclusion

In this uncontrolled, single-center complete-case series, use of a liquid berberine-containing combination preparation was associated with lower follow-up UDFF among 20 patients with paired measurements. The findings do not establish efficacy, safety, enhanced bioavailability, or an effect attributable specifically to berberine. Attrition, unblinded measurement, variable follow-up, incomplete confounder data, regression to the mean, absence of a control group, and commercial conflicts require cautious interpretation. The observations are hypothesis-generating and require confirmation in an independent randomized controlled trial.

What is new?

This is the first reported observational series examining a low-dose liquid berberine preparation (200 mg/day berberine hydrochloride) in adults with ultrasonographically confirmed hepatic steatosis, quantified by UDFF at paired timepoints. The series documents a consistent, quantitatively measured reduction in hepatic fat fraction across all 20 patients over a median of 7 weeks in a real-world general-practice setting, generating a hypothesis for controlled evaluation of liquid berberine formulations at comparatively low doses.

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List of Abbreviations

AI	Artificial intelligence	
ALT	Alanine aminotransferase	
AST	Aspartate aminotransferase	
BMI	Body mass index	
CI	Confidence interval	
FLI	Fatty Liver Index	
FU	Follow-up	
GGT	Gamma-glutamyl transferase	
GLP-1	Glucagon-like peptide-1	
HCl	Hydrochloride	
MASLD	Metabolic dysfunction-associated steatotic liver disease	
MRI	magnetic resonance imaging	
MRI-PDFF	Magnetic resonance imaging proton density fat fraction	
MRS	Magnetic resonance spectroscopy	
NAFLD	Non-alcoholic fatty liver disease	
NASH	Non-alcoholic steatohepatitis	
pp	Percentage points	
RCT	Randomized controlled trial	
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology	
UDFF	Ultrasound-derived fat fraction	
U/L	Units per liter.	

Conflict of interest/disclosure

B. Sikora, A. Magg, and B. Bahadori hold shares in BerBerSan®, the manufacturer of the investigational preparation (Berberstin), and participated in conceptualization, data collection, and drafting (see Author Contributions). B. Malekian, the corresponding author, has no financial or employment relationship with BerBerSan GmbH; data curation and formal analysis were performed by B. Malekian independently of the shareholder-authors, and figures/statistics were independently reproduced (see Outcomes and statistics). O. Lammel, A. Gächter, M. Moghadasian, and N. Moghadasian declare no competing interests. Despite this independent verification, the involvement of shareholder-authors in study conception and drafting is a material limitation; the manuscript is written to be descriptive and non-promotional, null and unfavorable findings are reported, and the preparation is not presented as an established or approved treatment.

Data availability

All de-identified patient-level UDFF values underlying the primary analysis are reported in Table 1, and the available baseline data for the five patients without follow-up are reported in Supplementary Table S1. Additional de-identified data and analysis materials are available from the corresponding author upon reasonable request, subject to applicable data-protection and consent requirements.

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B. Bahadori) participated in conceptualization, data collection, and manuscript drafting, as detailed in Author Contributions.

Consent for publication

All patients provided written informed consent for the use and publication of their anonymized clinical data and images.

Ethics approval

The authors determined that this retrospective analysis of de-identified routine-care data did not constitute a clinical trial under the Austrian Medicines Act. No prospective ethics-committee review or formal exemption determination was obtained. All patients provided written informed consent for the use and publication of their anonymized clinical data and images.

Commercial involvement and case selection

B. Bahadori, who participated in patient care and referral, is a shareholder in BerBerSan GmbH. The preparation was used voluntarily during routine clinical care and was not assigned according to a research protocol. Detailed information regarding how the preparation was initially offered or recommended and whether individual patients purchased or otherwise received it was not systematically documented in the retrospective dataset. The source cohort comprised 25 consecutive patients who used the preparation and underwent baseline UDF measurement. The primary analysis included the 20 patients with available paired follow-up measurements; the five patients without follow-up are described separately in Supplementary Table S1. No patient was selected or omitted according to the direction or magnitude of a known follow-up result.

Author contributions

B. Sikora: conceptualization, methodology, writing original draft, O. Lammel: investigation (clinical assessment and ultrasound examinations), data curation. B. Bahadori: investigation (patient care, referral), resources. B. Malekian: data curation, formal analysis. A. Magg: project administration, resources. M. Moghadasian and A. Gächter: methodology, writing, review and editing. N. Moghadasian: writing, review and editing. All authors reviewed and approved the final manuscript.

Trademarks

BerBerSan® is a registered trademark of BerBerSan GmbH, Austria. ACUSON Sequoia is a trademark of Siemens Healthineers. Trade names are used for identification only and do not imply endorsement.

Author details

Bernhard Sikora¹, Babak Malekian², Agnieszka Magg³, Nikon Moghadasian⁴, Mohammed Moghadasian⁵, Oliver Lammel⁶, Afsaneh Gächter⁷, Babak Bahadori⁸

1. BerBerSan GmbH, Pfarrgasse, Schladming, Austria
2. Department of Ecosystem Management, Climate and Biodiversity, the University of Natural Resources and Life Sciences (BOKU), Vienna, Austria
3. Schladming, Austria
4. Independent Researcher, Winnipeg, Canada
5. Department of Food and Human Nutritional Sciences, and Canadian Centre for Agri-Food Research in Health and Medicine, Winnipeg, Canada
6. General Practice (Ordination Dr. Oliver Lammel), Ramsau, Austria

7. Department of Psychosomatic Medicine and Psychotherapy, University for Continuing Education Krems, Krems an der Donau, Austria
8. BahaMed Medical Centre, Schladming, Austria

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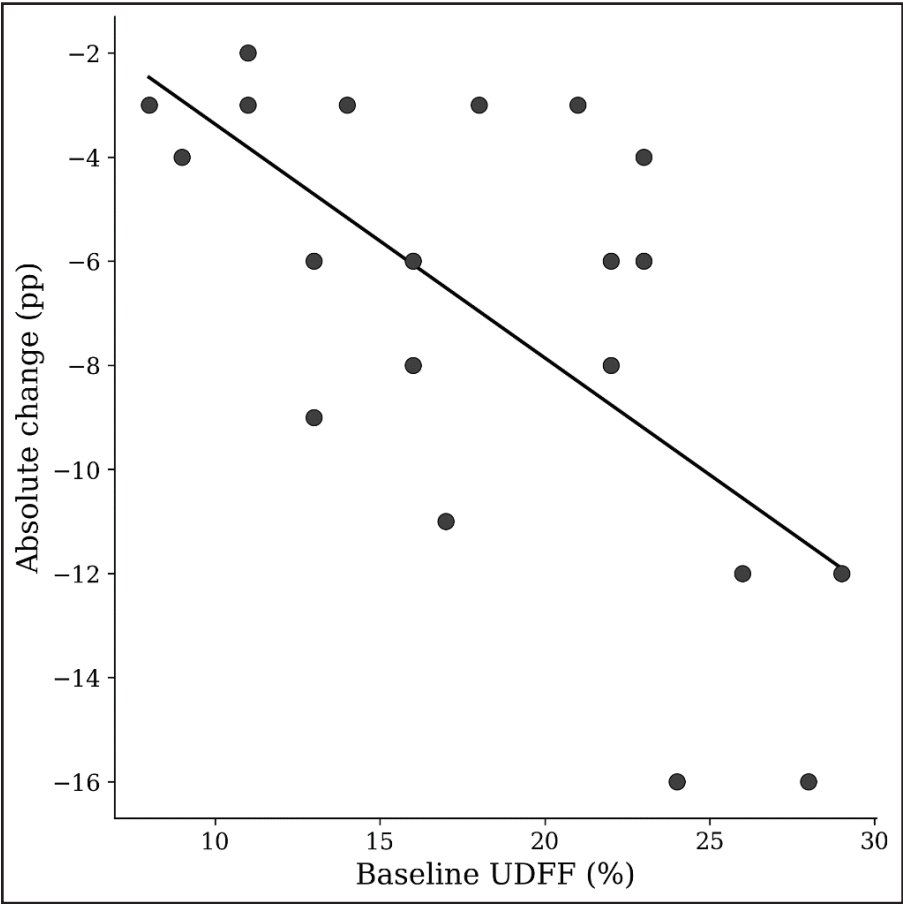
Summary of the case

1	Patient (gender, age)	16 male, 4 female; mean age 57 years (range 29-72)
2	Final diagnosis	Hepatic steatosis (UDFF $\geq 5\%$)
3	Symptoms	Incidentally detected hepatic steatosis; no acute symptoms
4	Medications	Berberstin (berberine HCl, 200 mg/day, liquid)
5	Clinical procedure	Quantitative ultrasound (UDFF; Siemens ACUSON Sequoia)
6	Specialty	Hepatology / General Practice

Supplementary Table S1. Available baseline characteristics of the five patients without follow-up UDFF measurements. These patients were not included in the paired complete-case analysis. NF, no follow-up; UDFF, ultrasound-derived fat fraction.

PATIENT	SEX	AGE (YEARS)	BASELINE UDFF (%)	BASELINE DATE
NF01	M	49	15	25 November 2025
NF02	F	62	21	3 December 2025
NF03	F	62	20	2 February 2026
NF04	M	69	27	27 March 2026
NF05	F	61	27	5 May 2026
Summary	2 M/3 F	Mean 60.6	Mean 22.0; median 21; range 15 to 27	N/A

UDFF = ultrasound derived fat fraction; M, male; F, female; NF, no follow-up.



Supplementary Figure S1. Relationship between baseline hepatic fat fraction and absolute change in UDFF (n = 20). Each point represents one patient. The line shows the linear fit between baseline UDFF and the absolute change observed at follow-up.