



1

Learning Objectives

- Identify commonly used complementary and alternative therapies in IBD
- Evaluate the evidence behind selected complementary and alternative therapies for induction and maintenance of remission in IBD
- Formulate an individualized, shared decision-making approach to incorporating complementary and alternative therapies into comprehensive IBD management

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2

2

Definitions – Complementary and Alternative (CAM) Medicines or Therapies

Complementary	Alternative
Using a non-mainstream approach together with conventional medicine	Using a non-mainstream approach in place of conventional medicine
Many providers comfortable with this approach	Can delay initiation of effective and established treatment for patients

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3

Types of Complementary and Alternative Therapies

- Natural or Biologically Based Therapy
 - Cannabis
 - Herbals (curcumin, indigo)
 - Vitamins, Minerals
 - Low dose Naltrexone
- Probiotics + Prebiotics
- Fecal Microbiota Transplant (FMT)
- Mind Body Therapies
 - Acupuncture, massage therapy, yoga, hypnotherapy, meditation, exercise, relaxation techniques
- Diets
- Peptides

NCCAM. <http://nccam.nih.gov/health/whatiscam>

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Use of CAM is common in IBD patients

- Most IBD patients have used or are used CAM or are interested in learning more
- May underreport due to fears, concerns about judgment

Methodological concerns

- Few randomized or controlled studies
- Small sample sizes
- Inadequate blinding
- Weak data, even with positive studies
- Lack of follow up studies

When evaluating CAM therapy, focus on:

- Study population** (UC, CD, Pouchitis, and disease severity)
- Outcome:** induction or maintenance of remission (clinical, endoscopic) or response
- Whether they are being used as **complementary** or **alternative** medicine
- Quality of **evidence**

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Prebiotics –

Study - Psyllium	Result
Maintenance of remission of UC	RCT, 105 pts, psyllium vs. Mesalamine vs combo Small unblinded RCT – lower treatment failure with psyllium + mesalamine (28%) vs mesalamine (35%)
Symptom improvement in UC in remission	Improved symptoms versus placebo for UC pts in remission (69 vs 24%)
Crohn's disease	No significant benefit for induction or maintenance of remission

The Bottom Line: Psyllium may help maintain remission and improve symptoms in UC. No benefit in Crohn's disease.

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Probiotics in IBD

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Crohn's Disease	Ulcerative Colitis
Overall data does not support the clinical effectiveness of probiotics for induction or maintenance of remission in CD	2 systematic reviews of studies since 2009 found insufficient evidence to support the use of probiotics for induction or maintenance of remission in UC
Post-operative recurrence – no demonstrated benefit RCT of VSL#3 vs. placebo for post-op prevention after ICR	Miele et al (2009): n=29 patients with new dx UC on steroids → 5ASA. VSL #3 (14) v placebo (15) • 1 yr: remission (93% VSL#3) v 36% (placebo) Sood et al (2009): n=77 • 6wk: VSL#3 is more effective in decreasing UCDAI by 50% (33% vs. 10%)
2020 AGA Guideline: Use only in the context of a clinical trial	2020 AGA Guideline: Use only in the context of a clinical trial (No recommendation, knowledge gap)

Miele et al, Am J Gastro 2009, 104:437.
 Sood et al, CGH 2009; 42:202
 Bresler et al, Gastro 2015; 1035
 Su et al, Gastroenterology 2020; 159:697

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Probiotics for Pouchitis

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Study	N	Study group	Dose	Result
Gionchetti (2000, Gastro)	20/20	Maintenance of remission in chronic pouchitis	6 g/day	Remission 85% of patients on VSL#3 at 9 months compared to 0% in placebo
Mimura (2004, Gut)	20/16	Maintenance of remission in chronic pouchitis	6 g/day	Remission in 85% of patients on VSL#3 at 12 months compared to 6% in placebo
Gionchetti (2003, Gastro)	20/20	Prophylaxis	3g/day	Acute pouchitis occurred in 10% in the VSL#3 group compared with 40% in the placebo group at 12 months

2024 AGA Pouchitis Clinical Practice Guidelines:
-No recommendation for primary prevention of pouchitis or treatment of pouchitis
-In patients with recurrent pouchitis that responds to antibiotics, recommend probiotics to prevent recurrent pouchitis
 Recommend De Simone Formulation used in clinical trials

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8

Curcumin for UC



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Study	Result
Lang et al (2015)	RTC Mild-to-moderate UC pts on 5ASA w/ no response @2w max tx n=50, randomized to 3g curcumin/d v placebo Results @4w: endo response (47.6% v 0.55%), endo remission (38% v 0.5%)
Sadeghi et al (2020)	RCT Mild-to-moderate UC pts on TNFa n=70, randomized to 1500mg curcumin/d v placebo Results @ 8w: ↓CRP, ESR, ↑IBDQ-9 Scores comp to placebo
Banerjee et al (2021)	RCT Mild-to-moderate UC pts on 5ASA n=69, randomized to 50mg bio-enhanced curcumin v placebo Results @ 6mo: 95% clinical remission vs. 0% clinical remission

The Bottom Line: May be useful as an adjunct therapy in mild-to-moderate UC
 Possible adverse effects: abnormal LFTs

Banerjee et al, J Clin GI 2021 Sep 1;55(8):702-708.
 Sadeghi et al, Phytother Res 2020; May;34(5):1123-1133.
 Lang et al, Clin Gastroenterol Hepatol. 2015 Aug;13(8):1444-9.e1.

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9

Curcumin for CD



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Study	Result
Bommelaer et al (2020)	RCT - CD patients after surgery n=60 on AZA, randomized to 3g curcumin/d v. placebo X 6 mo Terminated early due to futility No differences in clinical/endoscopic endpoints
Sugimoto et al (2020)	RTC Mild-to-moderate CD pts n=30, randomized to 360mg/d curcumin v placebo 12w results: 40% reduction in clinical, 15% reduction in endoscopic sx compared to 0% in the placebo group

The Bottom Line: Utility is less clear in Crohn's disease
Possible adverse effects: abnormal LFTs

Bommelaer et al, Clin GI & Hep 2020;18:1553-1560.
Sugimoto et al, JCC 2020; Dec Vol 14:12 1693-1701.

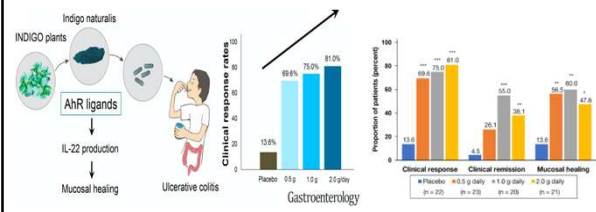
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CurQD in Ulcerative Colitis

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2018: Multicenter, double-blind trial, n=86



The diagram shows the mechanism of CurQD: Indigo plants → INDIGO plants → Indigo naturalis → AHR ligands → IL-22 production → Mucosal healing. It also shows a bar chart of clinical response rates for Placebo (13.6%), 55g (68.6%), 11g (75.0%), and 22g (81.0%).

Gastroenterology

Proportion of patients (percent)

Outcome	Placebo (n=25)	55g (n=25)	11g (n=25)	22g (n=21)
Clinical response	11.6	68.6	75.0	81.0
Clinical remission	4.8	26.1	35.1	55.0
Mucosal healing	13.6	58.5	66.7	71.4

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CurQD in Ulcerative Colitis— RCT 2024

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Ben-Horin et al. Curcumin-QingDai Combination for Patients with Active Ulcerative Colitis: A Randomized, Double Blinded, Placebo-Controlled Trial. Clin Gastro Hep 2024.

Methods

QingDai (QD) Curcumin

Combination herbal extracts of curcumin+QD (CurQD)

Patients with active UC (n=42, 48% immunomodulatory/biologic experienced)

8 weeks induction → 8 weeks Maintenance

Analysed (n=28) CurQD (n=28)

Analysed (n=18) Placebo

Primary outcome: Clinical response (SCCA drop of 1 point) and endoscopic Mayo 3 point or calprotectin 50% response

Results

Primary and most secondary outcomes better for CurQD compared to placebo at week 8

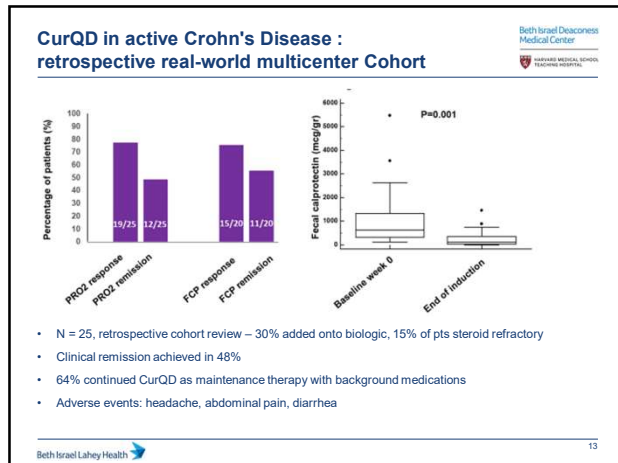
Maintenance with gut-directed curcumin alone is successful in most responding patients

Comparable safety

Safety dataset	CurQD (n=48)	Placebo (n=18)
Infection	2(4.2)	2(11.1)
Headache	2(4.2%)	2(11.1%)
Upper extremity elevation	3(6.3%)	1(5.6%)
Worsening of colitis	2(4.2%)	2(11.1%)
AKI requiring discontinuation	2(4.2%)	1(5.6%)
Discontinuation for Non-colitis AEs	2(4.2%)	2(11.1%)

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12



13

CurQD

The Bottom Line:

- CurQD
 - Active Ulcerative Colitis - RCT data
 - Induction of clinical response in active UC over placebo (85 vs 30%)
 - Induction of clinical remission in active UC over placebo (50 vs 8%)
 - Clinical response + objective evidence (endo or FCP – 43 vs 8%)
 - Endoscopic improvement over placebo (75 vs 20%)
 - Reduction of FCP > 50% (46 vs 15%)
 - Crohn's Disease – real world data
 - Induction of clinical remission (48%), clinical response (76%)
 - Decreases fecal calprotectin
 - If used for high doses for prolonged periods, associated with irreversible pulmonary hypertension (not seen in studies)

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Oral Aloe Vera Gel

Key Findings:

- One small positive randomized trial in mild to moderate UC
- 2004, n= 44 100 mL aloe vera gel orally twice daily x 4 weeks (n = 30) vs placebo (n = 14)
- Remission (primary, all non-significant):** aloe vs placebo — clinical 30% vs 7% (p = 0.09), endoscopic 27% vs 18% (p = 0.69), histological 29% vs 44% (p = 0.43).
- Clinical response (secondary, significant):** 47% vs 14% (p = 0.048).
- Tolerability:** well tolerated, mild adverse effects at rates similar to placebo.
- Side effects: diarrhea (+ blood), renal injury
- Very limited data
- Products not standardized

References:

- Langmead L, Feakins RM, Goldthorpe S, et al. Randomized, double-blind, placebo-controlled trial of oral aloe vera gel for active ulcerative colitis. *Aliment Pharmacol Ther.* 2004;19(7):739-47. d
- Guo X, Mei N. Aloe Vera: A Review of Toxicity and Adverse Clinical Effects. *J Environ Sci Health C Environ Carcinog Ecotoxicol Rev.* 2016;34(2):77-96.

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15

Omega 3 Fatty Acids: Fish Oil Maintenance of Remission in IBD

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Study	Result
Meta-Analysis – Maintenance in UC	3 trials showed no benefit in prevention of relapse vs placebo Loeschke et al, Hawthorne et al, Mantzaris et al – early reductions in relapse at 2-3 months that vanished by 2-3 years
Feagan et al (2008) Maintenance in CD	RCT x 2 (n = 189, n = 190) Maintenance of Remission for Crohn's disease – mild disease activity 4g/d of omega-3 free fatty acids or placebo Treatment was no effective in prevention of relapse of Crohn's Fish oil increased diarrhea and upper GI symptoms

The Bottom Line: Evidence shows no benefit in maintenance of remission in UC or Crohn's disease

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16

Low Dose Naltrexone

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Study	Result
LDN in Crohn's Disease (2026) Van de Pol et al.	Prematurely terminated multicenter, double blind, RCT Not effective for induction of remission in CD No clinical or endoscopic benefit over placebo (endoscopic remission higher in placebo group) Did reduce fatigue
Cochrane Meta-Analysis (2018): Induction of remission in CD	2 small RCTs (n=46 total) – 12 wk (adult) and 8 wk (peds) Adult trial trend towards clinical + endo response Peds within subject improvement in PCDAI, quality of life
CD and UC Lie et al (2018)	Observational NOT a RCT LDN 4.5 mg/d for 12 weeks in refractory CD and UC (not in remission) N = 47 – clinical improvement in 74%, remission 25%

The Bottom Line: No evidence of benefit for induction of remission in Crohn's disease. No RCT data for UC.

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17

17

Cannabis for Induction of Remission in IBD

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Crohn's Disease – Induction of Remission	- Inhaled THC (Naftali 2013 n = 21) - refractory CD – RCT, DB, PC - no difference in clinical remission, clinical response - Low dose oral CBD (Naftali 2017, n = 19), 10 mg BID, no clinical response over placebo
Ulcerative Colitis – Induction of Remission	- Inhaled THC (Naftali 2021 n = 32) – RCT, DB, PC 8 wks - THC w/ greater clinical response– improved QoL, clinical activity (# BM, abd pain), not difference in endo, biomarkers - CBD extract (Irving et al) 2018 – RCT, DB, PC – no difference in remission rates
Meta- Analysis 2025 (Kang et al)	- Statistically significant reduction in clinical disease activity in CD (RR -0.91, 95% CI -1.54 to -0.28) but not in UC (RR -2.13, 95% CI -4.80 to 0.55), and improved QoL in both - No difference in endoscopic disease activity or biomarkers

The Bottom Line: Cannabis and cannabinoids improve symptoms and quality of life in IBD but have not been shown to induce or maintain objective (endoscopic/biomarker) remission

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18

18

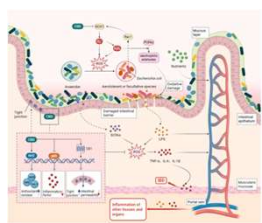
Cannabis

Safety Concerns

- THC content varies greatly (0.5% to 50%), and the optimal dosing/delivery method unclear
- Legal issues remain in many states

Many side effects

- Cannabinoid hyperemesis syndrome
- Increased risk of psychotic symptoms, panic, anxiety, tachycardia, hallucinations and delusions, potential for abuse, drugged driving, respiratory infections, stroke, MI
- Decrease in male and female infertility, IQ scores
- Edibles – accidental overdose due to slower onset of action



Doeve et al. J Clin Med 2021; Oct 13(50):798-808
Shaner et al. BMC Psychiatry 2014; 14: 472-480
Bergel et al. Pharmacotherapy 2013
Li AC et al. Epilepsia Rev 2012
Image: Lv et al. Redox Bio 2020

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19

Fecal Microbiota Transplant

Crohn's Disease – Induction of Remission	- Kao et al., AJG 2024; RCT, PC - mod CD, colon + capsule qwk terminated early for futility—0% (0/15) FMT vs 8.3% (1/11) placebo - combined clinical + endoscopic remission at wk 8 - RCT n = 17, steroid induced remission, higher steroid free remission, not significant
Ulcerative Colitis – Induction of Remission	- AGA's mild-mod UC guideline, 4 RCT pooled, n = 281 - FMT more effective than control at inducing clinical remission and endoscopic remission - AGA's 2024 FMT guideline, FMT more likely to achieve clinical remission than control, uncertain for endoscopic remission (15.6% vs 9.6%) and serious adverse events (7.3% vs 5.1%). 2026 updated meta-analysis of 16 RCTs - combined colonoscopy-plus-enema approach yielded the largest benefit (>2-fold remission rate)
Ulcerative Colitis - Maintenance	FMT-AID (Kedia et al Gut 2022): superior for 8 wk clinical response (65.7% vs 35.5%), remission (60% vs 32.3%), and deep remission (36.4% vs 8.7%)

The Bottom Line: FMT shows a reproducible induction signal in mild-to-moderate UC (best with intensive, multidonor, lower-GI protocols), is investigational, not recommended outside clinical trials. Failed to show benefit in Crohn's disease

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20

Appendectomy with standard medical therapy is superior in maintaining remission in UC

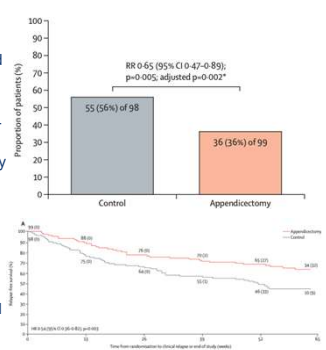
ACCURE: open label, international, randomized trial

UC patients in remission but had been treated for relapse within 12 months

Randomized to appendectomy + standard medical therapy (n = 101) or standard medical therapy (n = 100)

Primary outcome: disease relapse within 1 year- 36% vs 55%

Also more likely to maintain lower disease activity, reduce initiation of biologics, improved HR-QOL at 1 year



Relapse Rates:

Group	Relapse Rate (%)	n/N
Control	55	98/178
Appendectomy	36	36/99

RRR 0.65 (95% CI 0.47-0.89); p=0.005, adjusted p=0.002*

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21

My thoughts on CAM In IBD

- Meet your patient where they are
 - But suggest a middle ground that is evidence based
 - Recommend complementary and adjunctive therapy
- Ask about their concerns (ex: medication)
 - Listen and address
 - Validate their concerns and experiences
- Discuss benefits and risks of options
 - Discuss risks of undertreating
- Recommend overall health based therapies
 - Mediterranean diet, exercise, yoga, stress reduction, sleep, mental health support
- Use time based trials
- Use a multidisciplinary team



Photo Credit: Crohn's and Colitis Foundation Website

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22

Bottom Line

- Use evidence to discuss options for complementary therapies
- CurQD has shown efficacy in RCT for active UC
 - Induction of clinical response, remission, biomarker improvement and endoscopic improvement
- Use probiotics for secondary prevention in recurrent pouchitis that responds to antibiotics
- Psyllium husk in UC patients may help with symptoms
- Use shared decision making with time based trials



Photo Credit: Crohn's and Colitis Foundation Website

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23

23

Thank you !

Questions?

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24

24
