Review Paper

Systematic Review of Complementary and Alternative Medicine Treatments in Inflammatory Bowel Diseases

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Abstract

Objective: We performed a systematic review for Complementary and Alternative Medicine [CAM] as defined by the National Institute of Health in Inflammatory Bowel Disease [IBD], ie Crohn’s disease [CD] and ulcerative colitis [UC], with the exception of dietary and nutritional supplements, and manipulative therapies.

Methods: A computerized search of databases [Cochrane Library, Pubmed/Medline, PsychINFO, and Scopus] through March 2014 was performed. We screened the reference sections of original studies and systematic reviews in English language for CAM in IBD, CD and UC. Randomized controlled trials [RCT] and controlled trials [CT] were referred and assessed using the Cochrane risk of bias tool.

Results: A total of: 26 RCT and 3 CT for herbal medicine, eg aloe-vera gel, andrographis paniculata, artemisia absinthium, barley foodstuff, boswellia serrata, cannabis, curcumin, evening primrose oil, Myrrhinil intest®, plantago ovata, silymarin, sophora, tormentil, wheatgrass-juice and wormwood; 1 RCT for trichuris suis ovata; 7 RCT for mind/body interventions such as lifestyle modification, hypnotherapy, relaxation training and mindfulness; and 2 RCT in acupuncture; were found. Risk of bias was quite heterogeneous. Best evidence was found for herbal therapy, ie plantago ovata and curcumin in UC maintenance therapy, wormwood in CD, mind/body therapy and self-intervention in UC, and acupuncture in UC and CD.

Conclusions: Complementary and alternative therapies might be effective for the treatment of inflammatory bowel diseases; however, given the low number of trials and the heterogeneous methodological quality of trials, further in-depth research is necessary.

Keywords: Ulcerative colitis, Crohn’s disease, CAM, complementary and alternative medicine, review
1. Introduction

Patients with inflammatory bowel disease [IBD] rank among the highest users of complementary and alternative medicines [CAM], with current or past use of CAM ranging from 21–60%.1–3 Their primary motivations include an inadequate response to available medications or concerns over side effects.

The use of complementary and alternative medicine [CAM] is widespread in Western Europe and North America,1–3 particularly by those individuals with chronic diseases.12–15 The National Center for Complementary and Alternative Medicine defines CAM as a group of diverse medical systems, practises and products that are not presently considered to be part of conventional medicine.16 The term ‘alternative medicine’, furthermore, implies that this is used instead of, and the term ‘complementary medicine’ that this is used integrated with, conventional medicine. As we demonstrated in our previous work, only 48.1% of IBD patients regarded a scientific foundation for CAM treatments as being important.8 Indeed, a considerable proportion would use a CAM treatment even if research proved that it yields negative results, indicating that physicians’ reasons for therapy differ from those of patients.9

Often commonly used approaches are supported by little or no valid scientific studies. Greater interest in CAM worldwide has led to increased scientific investigation in the field.10–13 We performed a systematic review for Complementary and Alternative Medicine [CAM], as defined by the National Institute of Health in Inflammatory Bowel Disease [IBD], i.e. Crohn’s disease [CD] and ulcerative colitis [UC], with the exception of dietary and nutritional supplements. The possibility of meta-analysis was considered separately for every field of CAM presented but could not be performed due to heterogeneous study designs and outcome measures. Inflammatory bowel diseases like Crohn’s disease and ulcerative colitis [UC] are chronic relapsing diseases. Though recent progress in research has deepened our understanding of the diseases, there is no cure to date. Chronic therapy for IBD is needed given the difficulty of predicting and controlling the frequency and severity of disease exacerbations. In addition, a significant proportion of patients are not sufficiently helped by conventional therapy or suffer from relevant adverse events. This paper aims to identify and review RCTs on CAM in IBD and offer an overview of the field with tables, and a summary of the evidence in the different CAM categories.

2. Methods

2.1. Protocol and registration

This review was planned and conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [PRISMA].17 The protocol was not registered on any database.

2.2. Eligibility criteria

To be eligible for review, studies were required to meet the following conditions:

1) Types of study designs: controlled clinical trials, randomized controlled trials, randomized controlled cross-over trials, cluster randomized trials. Studies that investigated the effects of therapies within one group only [eg dosage-finding studies] were not considered eligible.

2) Types of participants: Studies of patients diagnosed with ulcerative colitis and/or Crohn’s disease were eligible, regardless of age, condition’s duration or the state [remission, active]. Studies were not included if IBS was not the targeted disease but was associated with the targeted disease. No restrictions regarding diagnostic procedures were applied.

3) Types of interventions: Studies that investigated CAM therapies according to the NIH definition18 were eligible. These included natural products such as herbs, botanicals, or helminthes; mind/body interventions such as meditation, relaxation techniques, stress management except for psychotherapy, mindfulness-based stress reduction, comprehensive lifestyle modification programs, hypnosis, yoga, tai chi or qigong, fasting, traditional Chinese medicine interventions, ayurvedic, anthroposophic or homeopathic therapies, balneotherapy, acupuncture, acupuncture and cataplasm. Massage and manipulative therapies were beyond the scope of this review and not included. Studies investigating probiotics or omega-3 fatty acids, fish oils, or essential oils as well as vitamins and minerals were also excluded.

4) Types of outcomes: Studies were eligible if they assessed at least one of the following outcomes: induction or maintenance of remission, disease activity or symptom severity, quality of life, or psychological variables. Safety would also be addressed.

5) Length of follow-up: No restrictions regarding length of follow-up were applied.

6) Accessibility of data: Studies were eligible only if they were published as full papers, and only English or German language publications were considered eligible.

2.3. Literature search

The following electronic databases were searched through to March 12, 2014: Pubmed/MEDLINE, Scopus, Cochrane central register of controlled trials and PsychInfo. The literature search, which was constructed around search terms for ulcerative colitis/Crohn’s disease and CAM therapies, was adapted for each database as necessary. The complete search strategy used on the Pubmed/MEDLINE database is shown in Box 1.

The search was limited to articles in English and German and to studies with adult humans and was adapted for the other databases accordingly.

Two reviewers screened the abstracts of the candidate studies individually. The selected studies were then checked in detail on evaluation of the full manuscript, with eligible papers being included in the systematic review.

Two reviewers independently extracted data on studies’ characteristics [participants, interventions, control conditions, co-interventions, outcome measures, results]. Disagreements were checked with a third reviewer and resolved by agreement.

The risk of bias at study level was assessed by two independent reviewers using the 2006 Method guidelines for systematic reviews of the Cochrane Musculoskeletal Group.19 These guidelines recommend the imposition of seven quality criteria, each of which is rated as ‘low risk’, ‘high risk’, or ‘unclear risk of bias’. These criteria relate to the following risk-of-bias categories: random sequence generation [selection bias], allocation concealment [selection bias], blinding of participants and personnel [performance bias], blinding of outcome assessors [detection bias], incomplete outcome data [attrition bias], selective reporting [reporting bias], and other bias relating to major study flaws.

If study data were inconclusive, trial authors were contacted for further study details. Studies that scored positive on at least 6 of the 12 criteria and had no serious flaw were rated as having low risk of bias. Studies that met fewer than 6 criteria or showed a serious flaw were rated as having high risk of bias.19
3. Results

3.1. Literature search

The literature search [Figure 1] yielded a total of 1729 papers, with 263 duplicates, leaving 1466 hits for abstract screening. After abstract screening, 35 studies were considered potentially eligible and read in full text. After exclusion of another 6 full-text articles, 29 full-text articles were included in the systematic review.

Of those, 29 studies were identified for this review; 26 of them were RCTs, and 3 were non-randomized ILED trials. Trials were categorized in distinct groups: herbs and botanicals [n = 19]; mind/body medicine [n = 7]; acupuncture [n = 2], and trichuris suis ova [n = 1]. The targeted diseases included ulcerative colitis [n = 20], Crohn’s disease [n = 6] or inflammatory bowel disease [both UC or CD] [n = 3]. The study sizes ranged from 22 to 224 patients, allocated to 2 or 3 groups respectively. Studies details are presented in Table 1.

The risk of bias [Table 2] was quite heterogeneous, from studies with a high risk in almost all domains to studies with no apparent risk of bias in any domain. The most critical domains for risk of bias were random sequence generation and allocation concealment, with one-third of the studies not reporting adequate methods. Data on compliance were not provided in almost half of the trials. Blinding of participants, providers, and outcome assessors was satisfactory in trials on herbal medicine, but not feasible in trials on behavioral interventions. Finally, although the drop-out rate in many trials was acceptable, only the minority of trials analyzed primary results in an intention-to-treat analysis.

3.1.1. Herbs and botanicals

Nineteen studies were identified evaluating herbs and botanicals in IBD, including studies on: boswellia serrata [n = 4]; artemisia absinthium [n = 2]; androgroplis paniculata [n = 2]; and curcumin [n = 2]; and 1 study each on aloe vera, cannabis, germinated barley, Myrrhinil intest®, plantago ovata, silimarina, sophora, super evening primrose, and wheat grass juice [Table 1].

3.1.2. Boswellia serrata [Indian frankincense]

Two randomized [30,31] and two non-randomized controlled trials [32,33] were available for boswellia serrata. They were tested in patients with ulcerative colitis [32,33] or Crohn’s disease [30,31] for active disease [30,32,33] or maintenance of remission. [31]

Gerhard et al. [30] investigated 102 patients who received either boswellia serrata or mesalazine in a double blind manner for 8 weeks. At Week 8 there was no significant difference regarding disease activity or remission rates, and furthermore no serious adverse events had been observed.

Gupta et al. [32,33] tested the efficacy of different doses of boswellia serrata compared with sulfasalazine in two non-randomized studies; 42 [32] and 30 [33] patients with ulcerative colitis, respectively, received treatment for 6 weeks. The tested outcomes included remission, severity of IBD symptoms, and safety. None of the tested variables revealed any significant difference between the groups; adverse events included nausea, epigastric pain, heartburn and a lack of appetite, and were present in 6 of 42 and 2 of 30 patients, respectively.
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<tr>
<th>Author</th>
<th>Disease</th>
<th>No of subjects, no of groups</th>
<th>Study type</th>
<th>Intervention</th>
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<td><strong>HERBS AND BOTANICALS:</strong></td>
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<td>Gerhard, 2001</td>
<td>Active CD</td>
<td>102, 2 groups; [50 BS; 52 ME]</td>
<td>RCT</td>
<td>Boswellia serrata extract H15 [BS]; 3, 6g daily for 8 weeks</td>
<td>Mesalazine [ME]; 4,5g daily for 8 weeks</td>
<td>2, 4, 6, 8 weeks</td>
<td>1. CDAI 2. Remission 3. Adverse events</td>
<td>1, 2. n.s. 3. 8 patients in BS, 15 patients in ME; no serious adverse events</td>
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<td>Gupta, 1997</td>
<td>UC</td>
<td>42, 2 groups [34 BS, 8 SU]</td>
<td>Non-randomized</td>
<td>Boswellia serrata gum resin [BS]; 3 x 350mg daily for 6 weeks</td>
<td>Sulfasalazine [SU]; 3 x 1g daily for 6 weeks</td>
<td>6 weeks</td>
<td>1. Remission 2. Abdominal pain 3. Sigmoidoscopic examination 4. Rectal biopsy 5. Stool sample 6. Grading of colitis 7. Body weight 8. Laboratory testing: Hb, iron, phosphorus, calcium, protein, leukocytes, eosinophils 9. Adverse events</td>
<td>1, 2, 3, 4, 5, 6, 7, 8. n.s. 9. 6 patients in BS; no serious adverse events</td>
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<tr>
<td>Gupta, 2001</td>
<td>UC</td>
<td>30, 2 groups; [20 BS, 10 SU]</td>
<td>Non-randomized</td>
<td>Boswellia serrata gum resin [BS]; 3 x 300mg daily for 6 weeks</td>
<td>Sulfasalazine [SU]; 3 x 1g daily for 6 weeks</td>
<td>6 weeks</td>
<td>1. Remission 2. Abdominal pain 3. Sigmoidoscopic examination 4. Rectal biopsy 5. Stool sample 6. Grading of colitis 7. Body weight 8. Laboratory testing: Hb, iron, phosphorus, calcium, protein, leukocytes, eosinophils 9. Adverse events</td>
<td>1, 2, 3, 4, 5, 6, 7, 8. n.s. 9. 2 patients in BS; no serious adverse events</td>
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<tr>
<td>Holtmeier, 2010</td>
<td>CD in clinical remission</td>
<td>82, 2 groups [42 BS, 40 Placebo]</td>
<td>RCT</td>
<td>Boswellia serrata extract PS0201Bo [BS]; 6 x 400mg daily for 12 months</td>
<td>Placebo; For 12 months</td>
<td>4, 16, 28, 40, 52, 64 weeks</td>
<td>1. Maintenance of remission 2. Time to relapse 3. CDAI 4. IBDQ 5. Adverse events</td>
<td>1. n. s. 2. n. s. 3. n. s. 4. n. s. 5. 29 patients in BS, 34 patients in Placebo; no serious adverse events</td>
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<td>Author</td>
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<tr>
<td>Artemisia absinthium</td>
<td>Active UC</td>
<td>224, 3 groups [75 HMPL1, 74 HMPL2, 75 Placebo]</td>
<td>RCT placebo-controlled double-blinded</td>
<td>Andrographis paniculata extract [HMPL-004] HMPL 1: 1200 mg HMPL 2: 1800 mg 3 doses daily for 8 weeks + stable dose of mesalamine</td>
<td>Placebo + stable dose of mesalamine</td>
<td>8 weeks</td>
<td>1. Clinical response 2. Clinical remission 3. Mucosal healing 4. MAYO score 5. Safety</td>
<td>5. Sig. group difference in favor of HMPL 6. n.s. 7. n.s. 8. n.s. 9. 8% of patients in HMPL: similar, except for mild rashes, 2 adverse events in each group</td>
</tr>
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<td>Omer</td>
<td>CD</td>
<td>40, 2 groups [20 AA, 20 Placebo]</td>
<td>RCT Placebo-controlled Double-blinded</td>
<td>Artemisia absinthium [AA]; 6 x 230mg daily for 10 weeks; in addition to steroid or prednisolone [constant dose until Week 2, gradually reduced dose until free of steroids in Week 10]</td>
<td>Placebo; in addition to steroid or prednisolone [constant dose until Week 2, gradually reduced dose until free of steroids in Week 10]</td>
<td>2, 4, 6, 8, 10, 12, 16, 20</td>
<td>1. CDAI 2. IBDQ 3. HAMD 4. Subjective well-being [VAS]</td>
<td>1. Sig. decrease in CDAI in AA after Weeks 6, 8, 20 compared with Placebo 2. n.s. 3. n.s. 4. Sig. increase in VAS in AA after 8, 10, 12 weeks compared with Placebo</td>
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<td>Sandborn, 2013</td>
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<td>Tang, 2011</td>
<td>Active UC</td>
<td>120, 2 groups [60 AP, 60 ME]</td>
<td>RCT Controlled?</td>
<td>Andrographis paniculata, HMPL-2004 [AP]; 3 x 400mg daily for 8 weeks</td>
<td>Mesalazine [ME]; 3 x 1500mg daily for 8 weeks</td>
<td>2, 4, 6, 8 weeks</td>
<td>1. Clinical efficacy [DAI] 2. Endoscopic efficacy [EI] 3. Histologic efficacy</td>
<td>1. Sig. overall efficacy in AP and ME after 8 weeks compared with baseline 2. Sig. overall efficacy in AP and ME after 8 weeks compared with baseline 3. Sig. improvement in AP and ME after 8 weeks compared with baseline</td>
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<td>Hanai, 2006</td>
<td>Quiescent UC</td>
<td>89, 2 groups [45 CU, 44 Placebo]</td>
<td>RCT Placebo-controlled</td>
<td>Curcumin [CU]; 2g daily for 6 months; in addition to Sulfasalazine, 13g, or Mesalamine, 1.53 g</td>
<td>Placebo in addition to Sulfasalazine, 13g, or Mesalamine, 1.53g, for 6 months</td>
<td>2, 4, 6, 12 months</td>
<td>1. CAI 2. Endoscopic index 3. Recurrence rate 4. Adverse events</td>
<td>1, 2, 3. Sig. lower in CU compared with Placebo at 6 months 4. 7 patients; no serious adverse events</td>
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<td>Singla, 2014</td>
<td>Mild-to-moderate active UC</td>
<td>43, 2 groups [23 curcuma, 22 Placebo]</td>
<td>RCT Placebo-controlled</td>
<td>NCB-02 [curcuma longa; 72% curcumin, 18% demethoxy curcumin, 9% bis-demethoxy curcumin] enema [140mg in 20ml of water] once daily for 8 weeks + 800mg oral mesalamine twice daily</td>
<td>Placebo enema enema [140mg in 20ml of water] once daily for 8 weeks + 800mg oral mesalamine twice daily</td>
<td>8 weeks</td>
<td>1. Disease activity [UCDAI] 2. Remission rate [UCDAI &lt;3] 3. Endoscopic disease activity 4. Adverse events</td>
<td>1. n.s. 2. n.s. 3. n.s. 4. n.s.</td>
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<td>Ben-Arye, 2002</td>
<td>Active distal UC</td>
<td>24, 2 groups; [12 WG; 12 Placebo]</td>
<td>RCT Placebo-controlled Double-blinded</td>
<td>Wheat Grass Juice [WG]; 100 ml daily for 4 weeks [starting with 20 ml and increasing the dose by 20 ml each day until 100 ml]</td>
<td>Placebo; 100 ml daily for 4 weeks [starting with 20 ml and increasing the dose by 20 ml each day until 100 ml]</td>
<td>4 weeks</td>
<td>1. DAI score</td>
<td>1, 2, 5, 6, 8. Sig. differences in favor of WG</td>
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<td>2. Rectal bleeding</td>
<td>3, 4, 7, 9, 10. n.s.</td>
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<td>Fernandez-Banares, 1999</td>
<td>UC in remission</td>
<td>102, 3 groups; [35 PO; 37 ME; 30 PO + ME]</td>
<td>RCT Verum-controlled Open-label</td>
<td>Plantago ovata seeds [PO]; 20 g daily for up to 12 months</td>
<td>Mesalamine [ME]; 1.5 g daily Plantago ovata + Mesalamine [PO + ME]</td>
<td>3, 6, 9, 12 months</td>
<td>1. Maintenance of remission</td>
<td>1. n.s. after 12 months</td>
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<td>2. SCFA production [short-chain fatty acid]</td>
<td>2. Sig. increase in butyrate concentrations in PO group</td>
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<td>3. Adverse events</td>
<td>3. 5 patients in PO, 4 patients in ME, 6 patients in PO + ME; no serious adverse events related to trial therapy</td>
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<td>Greenfield, 1992</td>
<td>UC</td>
<td>43, 3 groups; [8 Olive oil, 16 MaxEPA, 19 SEPO]</td>
<td>RCT Placebo-controlled Double-blinded</td>
<td>Super evening primrose oil [SEPO]; 12 x 250 mg daily for 1 month, 6 x 250 mg for 5 months</td>
<td>Olive oil [Placebo]; 1 g daily for 6 months MaxEPA; 1 g daily for 6 months</td>
<td>6, 9 months</td>
<td>1. Stool frequency</td>
<td>1, 3, 4, 5, 6, 7. n.s.</td>
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<td>2. Stool consistency</td>
<td>2. Sig. group difference in stool consistency after 6, 9 months</td>
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<td>4. Relapse</td>
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<td>5. Sigmoidoscopic score</td>
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<td>6. Histology</td>
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<td>7. Laboratory: blood count, sedimentation rate, fatty acid levels in red blood cell membrane</td>
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<td>Author, Year</td>
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<td>Hanai, 2004</td>
<td>UC</td>
<td>59, 2 groups [22 GBF, 37 ST]</td>
<td>Non-randomized Verum-controlled Open-label</td>
<td>Germinated Barley foodstuff [GBF]; 20g daily for 12 months; in addition standard treatment [5-ASA/steroids]</td>
<td>Standard treatment with 5-ASA/steroids [ST]; for 12 months</td>
<td>3, 6, 9, 12 months</td>
<td>1. Changes in the dose of 5-ASA and steroids 2. CAI 3. Endoscopic score 4. Cumulative recurrence rate</td>
<td>1. Ssig. decrease of steroid use in GBF at 3 months compared with ST 2. Ssig. lower CAI in GBF at 3, 6, 12 months compared with ST 3. n.s. 4. Ssig. lower rate in GBF compared with ST</td>
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<tr>
<td>Author</td>
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| Langmead, 2004 | Active UC | 44, 2 groups [30 AV, 14 Placebo] | RCT        | Aloe vera gel [AV]; 2 x 100 ml daily for 4 weeks [starting with 25 ml and increasing the dose by 25 ml each time until 100 ml] | Placebo; 2 x 100 ml daily for 4 weeks | 2, 4 weeks | 1. Remission [SCCAI]  
2. Improvement [SCCAI]  
3. Physician's global assessment  
4. IBDQ  
5. Sigmoidoscopic examination  
6. Histologic results  
7. Laboratory testing: Hb, platelet count, CRP, serum albumin  
8. Adverse events | 1. n.s.  
2. Sig. increase in AV after 4 weeks compared with baseline  
3. n.s.  
4. Sig. increase in Placebo after 4 weeks compared with baseline  
5. n.s.  
6. Sig. decrease in histologic score in AV after 4 weeks compared with baseline  
7. n.s.  
8. 6 patients in AV, 4 patients in Placebo; no serious adverse events |
| Naftali, 2013  | Active CD | 22, 2 groups [12 cannabis, 10 Placebo] | RCT        | Cannabis sativa cigarettes [115 mg THC each], twice daily for 8 weeks | Placebo cannabis cigarettes [<2 mg THC each], twice daily for 8 weeks | 2, 8, 10 weeks | 1. Remission rate [CDAI]  
2. Response rate [CDAI]  
3. C-reactive protein  
4. Quality of life [SF-36]  
5. Side effects | 1. n.s.  
2. Sig. larger response rate in cannabis [90%] vs. Placebo [40%]  
3. n.s.  
4. Sig. larger increase in cannabis  
5. n.s. |
| Rastegarpanah, 2012 | Inactive UC | 80, 2 groups [42 silymarin, 38 Placebo] | RCT        | Oral silymarin [140 mg] once daily for 6 months | Placebo once daily 6 months | 6 months | 1. Hemoglobin  
2. Erythrocyte sedimentation rate  
3. Symptoms [abdominal pain, diarrhea, fatigue, anorexia, joint or eye complications]  
4. Disease activity [DAI]  
5. Adverse events | 1. Sig. improvement in silymarin group only  
2. Sig. improvement in silymarin group only  
3. No outcomes reported  
4. Sig. improvement in silymarin group only  
5. n.s. |
| Tong, 2011     | UC       | 126, 3 groups [42 CSCC1, 42 CSCC2, 42 ME] | RCT        | Sophora Colon Soluble Capsules [CSCC]; CSCC1: 18 x 960 mg  
CSCC2: 12 x 960 mg daily for 8 weeks | Mesalazine [ME]; 4 x 250 mg daily for 8 weeks | 2, 4, 6, 8 weeks | 1. Clinical efficacy  
2. Fibrocolonoscopic examination  
3. Stool sample: red blood cells, white blood cells  
4. Safety | 1. n.s.  
2. n.s.  
3. n.s.  
4. 3 patients in CSCC1, 2 patients in CSCC2, 2 patients in ME, no serious adverse events |
<table>
<thead>
<tr>
<th>Author</th>
<th>Disease</th>
<th>No of subjects, no of groups</th>
<th>Study type</th>
<th>Intervention</th>
<th>Control / other interventions</th>
<th>Follow-up</th>
<th>Outcome measures</th>
<th>Results</th>
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<tbody>
<tr>
<td>Berrill, 2014</td>
<td>IBD</td>
<td>66, 2 groups [33 MCT, 33 SC]</td>
<td>RCT</td>
<td>Multi-convergent Therapy [MCT]; 6 x 40-min sessions over 16 weeks</td>
<td>Standard care [SC] 4, 8, 12 months</td>
<td>1. IBDQ</td>
<td>1. n.s.</td>
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<td>3. Medication escalations</td>
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<td>5. Coping [WCC]</td>
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<tr>
<td>Elsenbruch, 2006</td>
<td>UC</td>
<td>30; 2 groups [15 MBSR, 15 WL]</td>
<td>RCT</td>
<td>MBSR program [MBSR]; 6 h, 1 day a week for 10 weeks</td>
<td>Waiting list control group [WL]; usual care</td>
<td>2 4, 6, 10 weeks</td>
<td>1. Quality of life [IBDQ, SF-36]</td>
<td>1. Ssig. improvement in SF-36 Mental Health Scale, Psychological Health Sum Score and IBDQ Bowel Symptoms Scale after 10 weeks in MBSR compared with WL</td>
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<tr>
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<td>3. CAI</td>
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<tr>
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<td></td>
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<td></td>
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<td>4. Laboratory lymphocytes, TNF-α, catecholamine, cortisol, prolactin, growth hormones</td>
<td>4. n.s.</td>
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<tr>
<td>Jedel, 2014</td>
<td>UC</td>
<td>55, 2 groups [27 MBSR, 28 AC]</td>
<td>RCT</td>
<td>Mindfulness-Based Stress Reduction [MBSR]; 2.5 hours, once weekly + homework for 8 weeks</td>
<td>Attention control [AC]; once weekly + homework for 8 weeks</td>
<td>2, 6, 12 months</td>
<td>1. Disease status [Mayo UC-DAI]</td>
<td>1. n.s.</td>
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<td>2. Inflammatory markers [calprotectin, cytokines, CRP]</td>
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<td>3. IBDQ</td>
<td>3. n.s.</td>
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<td>5. Severity of flare-up [UC-DAI]</td>
<td>5. n.s.</td>
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<tr>
<td>Author</td>
<td>Disease</td>
<td>No of subjects, no of groups</td>
<td>Study type</td>
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<td>Outcome measures</td>
<td>Results</td>
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</table>
| Keefer, 2013 | Quiescent UC | 54, 2 [26 Hypnotherapy, 29 control group] | RCT        | Gut-directed hypnotherapy 7 x 40 min sessions, weekly + home practice for 12 months, 1–2 times weekly | Attention control, discussions about ‘the connection between mind and body in UC’ | 52 weeks  | 1. Maintenance of clinical remission  
2. Quality of life [IBDQ]  
3. Quality of life [SF-12]  
4. Perceived stress questionnaire [PSQ]  
5. Perceived health competence [PHCS]  
6. IBD Self Efficacy Scale [IBD-SES]  
7. Rating form of IBD Patients [RF-IPC]  
8. The medication adherence form [MAS]  
9. Adverse effects | 1. Sig. more patients in remission in hypnotherapy compared with control, sig. more days to clinical relapse in hypnotherapy  
2–8. n.s.  
9. No adverse effects |
| Milne, 1986  | IBD     | 80, 2 groups [40 each]       | RCT        | Stress management technique: 6 x 3-h training sessions, including planning skills, communication skills, autogenic training | Usual care | 4, 8, 12 months | 1. CDAI  
2. IBD stress index | 1. Sig. improvement within the treatment group, but not control group for all time points  
2. Sig. improvement within the treatment group, but not control group for all time points |
| Mizrahi, 2013 | IBD    | 56, 2 groups                | RCT        | Relaxation training [Relax], 3 sessions and CD for home practice | Waiting control group, usual care | 5 weeks   | 1. Pain [VAS]  
2. Anxiety [STAI]  
3. QOL [IBDQ]  
4. Depression [VAS]  
5. Mood [VAS]  
6. Stress [VAS] | 1. Sig. improvement in relax, but not WL  
2. Sig. improvement in relax, but not WL  
3. Sig. improvement in relax, but not WL  
4. Sig. improvement in relax, but not WL  
5. Sig. improvement in relax, but not WL  
6. Sig. improvement in relax, but not WL |
<table>
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<tr>
<th>Author</th>
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<th>Outcome measures</th>
<th>Results</th>
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</thead>
<tbody>
<tr>
<td>Langhorst, 2007 UC</td>
<td>UC</td>
<td>60, 2 groups</td>
<td>RCT</td>
<td>Life style modification ([MBSR]; 6h, 1 day a week for 10 weeks)</td>
<td>Waiting control group, usual care</td>
<td>3, 12 months</td>
<td>1. Quality of life [IBDQ, SF-36]</td>
<td>1. Sig. improvement in SF-36 physical functioning after 3 months in MBSR compared with WL</td>
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<td>2. Psychological distress [BSI]</td>
<td>2. Sig. reduction of BSI anxiety after 3 months in MBSR compared with WL</td>
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<td>4. Medication change</td>
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**ACUPUNCTURE**

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<tr>
<th>Author</th>
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<th>Study type</th>
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<th>Control / other interventions</th>
<th>Follow-up</th>
<th>Outcome measures</th>
<th>Results</th>
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</thead>
<tbody>
<tr>
<td>Joos, 2004</td>
<td>Active CD</td>
<td>54, 2 groups [27 TCM, 24 CG]</td>
<td>RCT</td>
<td>Acupuncture; + moxibustion [TCM]; 10 sessions in 4 weeks</td>
<td>Control group [CG]; Acupuncture at non-acupuncture points, 10 sessions in 4 weeks</td>
<td>4, 12 weeks</td>
<td>1. CDAI</td>
<td>1. Sig. decrease after 4 weeks in TCM compared with CG</td>
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<td></td>
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<td>2. Quality of life [IBDQ]</td>
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<td></td>
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<td>3. General well- being</td>
<td>3. Sig. increase after 4 weeks in TCM compared with CG</td>
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<td>4. Serum markers of inflammation [α,1-acid glycoprotein, CRP]</td>
<td>4. Sig. decrease in α,1-acid glycoprotein in TCM after 4 weeks compared with baseline</td>
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<td></td>
<td></td>
<td>5. Adverse events</td>
<td>5. 3 patients in TCM unrelated to trial therapy, 2 patients in CG; no serious adverse events</td>
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<tr>
<td>Author</td>
<td>Disease</td>
<td>No of subjects, no of groups</td>
<td>Study type</td>
<td>Intervention</td>
<td>Control / other interventions</td>
<td>Follow-up</td>
<td>Outcome measures</td>
<td>Results</td>
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<td>Joos, 2006</td>
<td>Active UC</td>
<td>29, 2 groups [15 TCM, 14 CG]</td>
<td>RCT Sham-controlled Single-blinded</td>
<td>Acupuncture; + moxibustion [TCM]; 10 sessions in 5 weeks</td>
<td>Control group [CG]; Acupuncture at non-acupuncture points, 10 sessions in 5 weeks</td>
<td>5, 16 weeks</td>
<td>1. CAI 2. Quality of life 3. General well-being 4. Serum markers of inflammation</td>
<td>1. Sig. decrease after 5 weeks in TCM compared with CG 2. Sig. increases after 5, 16 weeks in TCM and CG compared with baseline 3. Sig. increases after 5 weeks in TCM and CG compared with baseline 4. n.s.</td>
</tr>
<tr>
<td>Summers, 2005</td>
<td>Active UC</td>
<td>54, 2 groups [30 TSO, 24 Placebo]</td>
<td>RCT Placebo-controlled Double-blinded</td>
<td>Trichuris suis ova [TSO]; 2500x at 2-week intervals for 12 weeks</td>
<td>Placebo</td>
<td>2, 6, 12 weeks</td>
<td>1. UCDAI 2. Remission 3. Clinical Colitis Activity Index 4. Laboratory testing: blood count, erythrocyte sedimentation rate, CRP, liver profile 5. Stool examination: ova, parasites, bacterial pathogens, C difficile toxin 6. Side effects</td>
<td>1. Significant higher response rate in TSO compared with Placebo after 12 weeks 2. n.s. 3. Sig. decrease in TSO compared with Placebo after 8 and 12 weeks 4. n.s. 5. Negative for ova and parasites in TSO 6. 1 in TSO, 3 in Placebo; no serious adverse events related to trial therapy</td>
</tr>
</tbody>
</table>

Suggestions for definitions: CAM, Complementary and Alternative Medicine; IBD, Inflammatory Bowel Disease; CD, Crohn’s disease; UC, ulcerative colitis; RCT, Randomized controlled trials; CT, controlled trials; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines; CDAI, Crohn’s disease activity index; GAI, Colitis activity index; TCM, Traditional Chinese Medicine; IBDQ, inflammatory bowel disease questionnaire; ASA, Aminosalicylic Acid; SF-36, Short Form (36) Health Survey; PSQ, perceived stress questionnaire; RDHS, Revised Daily Hassle Scale; WCC, Ways of Coping Checklist; BDI, Beck depression inventory; PSS, Perceived stress scale; RF, Rating form of IBD patients; MAAS, Mindful Attention Awareness Scale; VAS, visual analogue scale; STAI, State-Trait-anxiety inventory; QOL, Quality of life; UCDAI, ulcerative colitis disease activity index.
<table>
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<th>Bias</th>
<th>Author, year</th>
<th>Selection bias:</th>
<th>Performance bias:</th>
<th>Attrition bias:</th>
<th>Reporting bias:</th>
<th>Detection bias:</th>
<th>Total risk:</th>
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<td>Adequate random sequence generation</td>
<td>Adequate allocation concealment</td>
<td>Adequate participant blinding</td>
<td>Adequate provider blinding</td>
<td>Acceptable and described drop-out rate</td>
<td>Inclusion of an intention-to-treat analysis</td>
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<td>HERBS AND BOTANICALS</td>
<td>Andrographis paniculata</td>
<td>yes</td>
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<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
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</table>
Holtmeier et al.\textsuperscript{34} investigated a boswellia extract in a double-blind placebo-controlled study in 82 patients with Crohn’s disease in remission. After 12 months there was no significant difference regarding maintenance of remission, relapse time, or severity of symptoms. Adverse events were reported in equal amount for both groups, none of which was regarded as of serious magnitude.

Study quality was diverse for boswellia serrata, with two studies having high risk of bias,\textsuperscript{2,15} and two studies with high scores.\textsuperscript{30,36} The main weaknesses of the studies were the heterogeneity of the sample in the non-randomized sample,\textsuperscript{41} high drop-out rates\textsuperscript{46} or the missing explanations/analysis of drop-outs,\textsuperscript{2,15} and the short follow-up periods.\textsuperscript{30,32,33}

### 3.1.3. Artemisia absinthium [wormwood]

Two randomized controlled trials\textsuperscript{41,48} investigated the effect of wormwood in active Crohn’s disease. Twenty patients were treated with standard treatment alone or with additional artemisia absinthium for 6 weeks in an open-label fashion.\textsuperscript{35} Patients in the intervention group showed significant decrease in disease activity and depression, and an increase in quality of life after 6 weeks. No such differences were found within the control group. The study also found significant reduction of TNF-$\alpha$ [tumor necrosis factor alpha] within the intervention group.

Omer et al.\textsuperscript{49} compared the efficacy of wormwood to a placebo, on top of a steroid or prednisolone treatment which was gradually reduced until patients were free of steroids at Week 10. Forty patients were followed for up to 20 weeks; outcomes included severity of symptoms, quality of life, depression, and subjective well-being. At Weeks 6, 8, and 20, the intervention group reported significantly less symptoms, and increased well-being at Weeks 8, 10 and 12. No further differences were observed.

Study quality was mixed. The biggest concerns were non-randomization,\textsuperscript{41} missing blinding,\textsuperscript{41} the short observational period,\textsuperscript{41,48} and the non-reporting of adverse events.

### 3.1.4. Andrographis paniculata [Indian echinacea]

A total of 120 patients with active ulcerative colitis were studied in a randomized double-blind trial by Tang.\textsuperscript{50} Patients in the intervention group received 8 weeks of HMPL-004, which contains an andrographis paniculata extract, whereas the control group received mesalazine. Clinical symptom severity and endoscopic and histological signs were assessed every 2 weeks. Results revealed that both groups showed significant improvements on all outcomes. Side effects were twice as prevalent in the mesalazine group compared with the intervention group, occurring in 27% and 13% of the patients, respectively. Although the study quality was relatively high, the authors did not describe the randomization procedure nor the compliance.

Another trial by Sandborn and colleagues\textsuperscript{10} investigated the effects of andrographis paniculata extract HMPL-004 in patients with active ulcerative colitis; 224 patients were randomized to either 1200 mg or 1800 mg of the trial medication or to placebo. All patients also received stable doses of mesalamine. Outcomes were assessed after 8 weeks. Patients receiving andrographis paniculata showed significant higher response rates, but no differences between the doses were found. Remission rates were also similar between the groups. Except for mild rashes, which were more common in the intervention groups, no differences regarding adverse events were found. Quality of the trials was very high.
3.1.5. Curcumin

Hanai\textsuperscript{28} compared curcumin with placebo in addition to sulfasalazine for maintenance of remission in ulcerative colitis; 89 patients were randomly assigned, and patients as well as providers were blinded. Treatment lasted 6 months and clinical and endoscopic disease activity, recurrence rate, and adverse events were tested up to 12 months. Results showed significantly less disease activity and lower recurrence rate at 6 months in the verum group. No serious adverse events were observed in the study. The risk of bias of the study was considered low.

Another study with low risk of bias compared curcumin enema combined with oral mesalamine with placebo enema combined with oral mesalamine, in 45 patients with distal ulcerative colitis with mild-to-moderate disease activity.\textsuperscript{30} At 8 weeks, this study found no significant differences regarding disease activity or remission rate when analyzing the intention-to-treat population. No severe adverse events occurred.

3.1.6. Wheatgrass juice

Wheat grass juice vs. placebo was compared in a randomized double-blind study\textsuperscript{26} in patients with active ulcerative colitis; 24 patients were evaluated by means of disease activity, symptoms severity, and adverse events. After 4 weeks of wheat grass juice administration, patients showed significantly less disease activity, less rectal bleeding and less abdominal pain. Physician’s global assessment was also in favor of the intervention group. No serious adverse events were observed. Risk of bias was very low, but analysis did not include drop-outs, and follow-up was too short. Blinding on the other hand was very well described and the authors also checked the credibility of the blinding at the end of the study.

3.1.7. Plantago ovata [Desert Indian wheat]

Plantago ovata [PO] seeds, mesalamine, or a combination of both were studied in patients with ulcerative colitis in remission, by Fernandez-Banares.\textsuperscript{29}

Patients \(n = 102\) were randomly allocated to intervention or two control groups, and they were monitored for up to 12 months. Maintenance of remission after 12 months did not reveal significant differences. Patients in the PO group showed increased butyrate concentrations in the stool, but no serious adverse events were observed. The study had a low risk of bias, but blinding, reporting, and analysis of drop-outs were inadequate.

3.1.8. Super evening primrose oil

Greenfield et al.\textsuperscript{31} compared the efficacy of evening primrose oil on active ulcerative colitis with placebo [olive oil] and high-dose omega-3 oil. Treatment lasted 6 months and outcomes were assessed at 6 and 9 months for 43 patients. Besides stool consistency after 6 and 9 months, no further significant differences could be observed. Adverse events were not reported. The study has a low risk of bias, but randomization was not adequately described, and blinding was not appropriately done.

3.1.9. Germinated barley

Hanai\textsuperscript{28} compared standard therapy alone with standard therapy plus germinated barley foodstuff for 12 months. Group allocation for the 59 patients with ulcerative colitis was not randomized and neither patients nor providers were blinded. After 3 months, patients in the combined group showed significant decrease of steroid use, and after 3, 6 and 12 months the severity of clinical symptoms and recurrence of UC in those achieving remission was significantly lower in the intervention group. Risk of bias was rather high, with the main deficiencies being lack of randomization, blinding, analysis of drop-outs, and reporting of adverse events.

3.1.10. Myrrh, chamomile extract, and coffee charcoal

A combination of myrrh, chamomile extract, and coffee charcoal [Myrrhinil intest\textsuperscript{®}] was tested in a double-blind double-dummy RCT by Langhorst et al.\textsuperscript{40} A total of 97 patients received either Myrrhinil intest \textsuperscript{®} or mesalazine for 12 months. Analysis revealed that the preparation was not inferior to mesalazine regarding clinical outcomes and safety. The trial was judged to have a very low risk of bias.

3.1.11. Aloe vera gel

A total of 44 with active ulcerative colitis were included in this double-blind placebo-controlled study.\textsuperscript{44} Two-thirds of the patients were randomized to the aloe vera group and received 4 weeks of aloe vera gel at increasing doses. Remission, symptoms severity, physician’s global assessment, quality of life, and laboratory measures were taken at 2 and 4 weeks. The intervention group showed significant improvements in clinical signs and quality of life at 4 weeks compared with baseline, with a reduction in histologic score as well. No serious adverse events were reported. The study was judged to have low risk of bias.

3.1.12. Cannabis

One double-blind study compared cannabis sativa cigarettes with placebo cigarettes from which tetra-hydrocannabinol [THC] was removed, in 22 patients with active Crohn’s disease.\textsuperscript{45} This study found significant group differences favoring cannabis over placebo for response rate [>100 reduction in Crohn’s disease activity index [CDAI] scores], and quality of life, but not for remission rate [CDAI <150] or reduction of C-reactive protein. Side effects did not differ significantly between groups. Whereas this study had a low overall risk of bias, randomization and allocation procedure was insufficiently reported and blinding of participants failed.

3.1.13. Silymarin

One study assessed the effects of oral silymarin compared with placebo in 80 patients with inactive ulcerative colitis.\textsuperscript{46} Whereas hemoglobin levels, erythrocyte sedimentation rate, and disease activity significantly improved in the silymarin group but not in the placebo group, no group differences were reported. Incidence of adverse reactions did not change in either group. The study had high risk of bias.


Tong et al.\textsuperscript{47} investigated the effect of sophora colon-soluble capsules compared with mesalazine, which were administered in a single-blind fashion. Two different doses of sophora were tested. The study duration was 8 weeks; outcomes were assessed every 2 weeks in 126 patients with ulcerative colitis. Results revealed no significant differences between groups regarding disease activity or laboratory measurements. No serious adverse events were observed. Risk of bias was low; the main concerns regarded missing description of randomization and allocation, blinding methods, and compliance as well as a short observational period.

3.2. Mind/body medicine

3.2.1. Lifestyle modification

Two studies investigated the effect of lifestyle modification programs on disease activity, quality of life, psychological parameters and laboratory profiles\textsuperscript{48,64} in 30\textsuperscript{28} and 60\textsuperscript{65} patients with ulcerative
colitis. Both studies applied a randomized wait-list controlled study design. The programs lasted 10 weeks each and outcomes were assessed after 10 weeks and 3 and 12 months. Results showed significant improvement in psychological quality of life after 10 weeks and 3 months, as well as significant reduction of anxiety after 3 months. Neither medication nor laboratory profiles showed any change. Risk of bias was low in both studies. In one study, however, the randomization had to be criticized, because three patients changed groups after allocation.

3.2.2. Mindfulness-based interventions
Two further studies investigated the effects of mindfulness-based interventions on 66 patients with either inactive ulcerative colitis or Crohn’s disease, and on 55 patients with inactive ulcerative colitis. One study compared one-to-one multi-convergent therapy plus standard care with standard care alone, and the other study compared mindfulness-based stress reduction courses with time/attention control courses. Whereas no study showed significant group differences regarding disease activity, relapse, or psychological variables in the main analysis, significant effects on quality of life were found in patients with additional irritable bowel syndrome-type symptoms, and also effects on stress and C-reactive protein in patients who flared during the course of the study. Risk of bias was high in one study and low in the other.

3.2.3. Hypnotherapy
Keefer et al. investigated the effects of gut-directed hypnotherapy, a program that was developed for irritable bowel syndrome. Patients received 7 weekly sessions of hypnotherapy compared with an attention/control group, and after 52 weeks they were significantly better in pain, anxiety, depression, mood, stress, and quality of life as well as significant reduction of anxiety after 3 months. Neither medication nor laboratory profiles showed any change. Risk of bias was low in both studies. In one study, however, the randomization had to be criticized, because three patients changed groups after allocation.

3.2.7. Trichuris suis ova
Trichuris suis ova, ie whipworm eggs, were tested by Summers et al. in a randomized placebo-controlled double-blind trial on active ulcerative colitis. Treatment included intake of the therapeutic agent for 12 weeks at 2-week intervals. Every 2 weeks the disease activity, remission, and laboratory measures were taken. Results revealed that higher response rates but not remission rates were observed regarding disease activity in the intervention group compared with placebo after 12 weeks. No serious adverse event was observed in this trial. The risk of bias was very low, and the study received full points for every criterion.

4. Discussion
This review found evidence from 29 trials on complementary and alternative therapies in the treatment of inflammatory bowel diseases. Whereas most studies tested the effects of herbal medicine and botanicals, there were also a large number of trials available for mind/body or psychological interventions, as well as acupuncture trials and a trial utilizing helminths. For most interventions no more than one or two trials were available. The risk of bias was quite heterogeneous among the trials.

4.1. Interpretation
4.1.1. Herbs and botanicals
The treatment with herbal preparations containing a variety of potential effective ingredients offers a possible multi-target approach. However, the huge range of biologically active compounds may even result in adverse effects. Based on in vitro studies, numerous individual chemicals derived from several different plants may have antibacterial, antioxidant, anticytokine, anti-spasmodic, and neuromodulatory actions. Of more importance, a variety of herbs show first evidence with performance at least equal to conventional treatment alone, or superior to placebo when used as complementary to conventional treatment in clinical studies. Most of these herbal therapies have been reported to have plausible mechanisms of action in IBD. For example, in vitro as well as small in vivo studies have shown the suppression of TNF-α by wormwood compared with placebo. Andrographis paniculata shows inhibiting potential against TNF-α, IL-1β, and NF-KB in an in vitro setting.

Boswellic acid, the major constituent of boswellia, was shown to inhibit NF-KB signaling pathways in macrophages in mouse model of psoriasis, markedly decreasing the production of the pro-inflammatory key cytokine TNF-α and the chemokine MCP-1. In addition, in vitro studies and animal models show that boswellic acid inhibits
5-lipoxygenase selectively and has anti-inflammatory and anti-proliferative effects. Unlike other non-steroidal anti-inflammatory drugs, however, boswellic acid fails to show analgesic or antipyretic effects. In addition, it does not cause gastric ulcers in animals. This suggests that the action of boswellic acid is likely through mechanisms other than the inhibition of prostaglandin synthesis.

Myrrh resin, Commiphora molmol, with its main ingredients furanosesquiterpene, diterpenoids, and volatile acids, has anti-inflammatory, antiphlogistic, antioxidative, antibacterial, and astrin
gent potential.

Chamomile dry extract of chamomile flowers, with its main ingredients volatile acids, flavonglykosides, and hydroxycuma
rines, has anti-inflammatory effects and has antibacterial, spasmolytic, and ulcer-protective potential. The combination has shown first promising evidence in maintenance therapy of ulcerative colitis.

Cannabinoids were found to ameliorate inflammation in a mouse model of colitis. An anti-inflammatory effect of can
nabinoids, mainly through the cannabinoid 2 receptor, has been stated. Cannabinoid exposure antagonizes release of prosta
glandins, histamine, and the matrix-active proteases from mast cells. The phagocytic function of macrophages is suppressed by cannabinoid exposure. It also suppresses inflammation by down-regulating the production of cytokines such as TNF-α, interferon-γ, and interleukin-1. Of interest, in the clinical trial of Naftali et al., it was observed in 14% of patients taking placebos that an improvement in inflammatory marker concentrations occurred, which was not seen in the cannabinoid group.

Several other drugs, like bilberry with its mayor component anthocyanin, have been shown to have anti-inflammatory potential in vitro and in vivo but no randomized controlled trials were found. Therefore, they were not included in this paper.

4.1.2. Mind/body medicine
Perceived stress is a significant predictor for flaring in UC, and the risk of experiencing exacerbation is multiplied by prolonged exposure to stress. Up to 70% of patients with inflammatory bowel disease regard stress as modifying for their disease, and 85% regard sufficient coping as having a positive impact on their course of disease. Therefore, studies testing effects of different interventions targeting stress and psychological well-being on the course of disease are urgently warranted.

First studies in the field of relaxation training introduce improvements on several side effects and psychosocial components in IBD and, in the field of hypnotherapy, effects on maintenance therapy in UC. However, additional confirming studies are yet to come. Furthermore, the currently available studies in mindfulness-based stress reduction (MBSR) are clearly not powered sufficiently to give a conclusive answer as to whether it is effective for maintenance treatment and prevention of relapse in ulcerative colitis. However, a high compliance and no relevant side effects were described. Positive brief effects occurred for health-related quality of life. Although patients do not benefit in general in terms of disease activity or laboratory parameters, the results of the study of Jedel et al. indicate that a subgroup of patients, namely those with higher stress levels, actually do. This might be of special importance in individuals with heightened physiological responses to stress, in whom MBSR interventions might prevent flare-up by minimizing the impact of stress on inflammatory cascades. In addition, mindbody interventions might actually be able to turn patients’ and practitioners’ perspectives away from a purely pathogenetical view to complementary salutogenic approaches. Patients in the MBSR intervention group demonstrated significantly better quality of life during a flare compared with flared controls. This quite unique finding introduces a new quality of treatment, improving patients’ resources and prepar

4.1.3. Traditional Chinese Medicine (TCM)/acupuncture
Acupuncture has been used for thousands of years to treat various medical conditions. It has been shown to be effective for treating various pain and gastrointestinal disorders, particularly nausea due to operation, chemotherapy, pregnancy, and motion sickness. Several other drugs, like bilberry with its mayor component anthocyanin, have been shown to have anti-inflammatory potential in vitro and in vivo but no randomized controlled trials were found. Therefore, they were not included in this paper.

Consequently, first studies with trichuris suis ova, i.e, whipworm eggs, showed some positive treatment effects in ulcerative colitis as well as Crohn’s disease. The treatment was rated as safe, which was later further confirmed by a small study of Sandborn et al. Currently, two large randomized placebo-controlled multi-center trials in Crohn’s disease, one in North America and one in Europe, have been reported in the press as being negative; whereas a study in UC is ongoing.
4.2. Limitations
This review has several limitations. First, due to the selection of trials published in English or German only, trials of traditional Chinese medicine were not considered. The validity of findings is further limited by the small number of trials, rendering meta-analyses impossible. Many interventions have not been subjected to randomized trials or even to studies on humans. Furthermore, most trials tested interventions for ulcerative colitis; therefore conclusions are mainly limited to patients with ulcerative colitis.

Finally, several systematic reviews and meta-analyses have been published recently, but these have mainly focussed on herbal medicines, and they have not used detailed risk of bias assessment. Although they included trials in languages other than English and German, the absolute number of trials was not that much higher. The recent review, however, was also not limited to herbal medicines compared to the search in the here presented study; it is therefore more comprehensive and potentially relevant for researchers and clinicians.

4.3. Conclusion
Addressing the fact that IBD are caused and upheld by multifactorial processes, which include genetic predisposition, immune dysregulation, barrier dysfunction and altered microbial flora, as well as environmental and lifestyle factors, it seems plausible that subgroups of patients might benefit from a tailored therapy with emphasis on individually differing modalities.

Whereas the various herbal treatment approaches in principle are using the same pathogenetic paradigm as conventional pharmacotherapy, TCM/acupuncture and, especially, mind/body medicine widen the spectrum of therapy and add a resource-oriented salutogenic dimension to introduce a multimodal integrative treatment approach.

Patients try to find the most effective and safest therapy for their disorder, including every available option for treatment. In this context, they are likely to perceive CAM and mainstream medicine as equally available treatment options, and to exercise their freedom of choice on their way to a consumer-driven optimal treatment.3

A more individualized multimodal treatment approach and further high-quality designs in health research are warranted, to help tailor the right individualized treatment modalities for IBD patients, include salutogenic approaches like MBSR, and appropriate trials to picture these.

Conflict of interest statement
None declared.

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References
Systematic Review of CAM in IBD


