eISSN (Online): 2598-0580

Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Modulation of Inflammatory and Regenerative Pathways by *Channa striata* Extract in End-to-End Anastomotic Wound Repair: A Systematic Review

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ARTICLE INFO

Keywords:
Anastomosis
Channa striata
Inflammation
Snakehead fish
Wound healing

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v9i4.1264

A B S T R A C T

Background: Intestinal anastomotic healing is a complex process, often complicated by inflammation and impaired regeneration, leading to leakage and stricture. *Channa striata* (snakehead fish) extract, traditionally used for wound healing, possesses bioactive compounds with potential anti-inflammatory and regenerative properties. This systematic review aimed to critically appraise the *in vivo* evidence for the effects of *Channa striata* extract on inflammatory and regenerative pathways in end-to-end anastomotic wound repair. **Methods:** A comprehensive search of PubMed/MEDLINE, Scopus, Web of Science, Embase, and Cochrane Library databases was conducted for studies published between 2013 and 2024. Inclusion criteria comprised *in vivo* studies using animal models with end-to-end intestinal anastomosis, evaluating *Channa striata* extract versus a control, and reporting on relevant inflammatory and regenerative markers. Data extraction and risk of bias assessment (using SYRCLE's tool) were performed. **Results:** Seven studies met the inclusion criteria. These studies, primarily using rat models, demonstrated that *Channa striata* extract significantly modulated key inflammatory and regenerative pathways. Specifically, the extract reduced pro-inflammatory cytokines, increased anti-inflammatory cytokines, enhanced growth factor expression, and promoted collagen deposition at the anastomotic site. These effects were associated with improved anastomotic bursting pressure and reduced leakage rates. Risk of bias varied across studies, with some limitations in blinding and allocation concealment. **Conclusion:** *Channa striata* extract shows promise as a therapeutic agent for promoting anastomotic healing by modulating key inflammatory and regenerative pathways. However, further high-quality, standardized studies are needed to confirm these findings, elucidate precise mechanisms, and optimize extract formulation and dosage before clinical translation.

1. Introduction

Intestinal anastomosis, a surgical procedure involving the reconnection of two intestinal segments, stands as a cornerstone of gastrointestinal surgery. This procedure is indispensable in addressing various conditions, including bowel resection due to cancer, inflammatory bowel disease, and traumatic injuries. Despite advancements in surgical techniques and perioperative care, anastomotic leakage persists as a significant complication, with occurrence rates ranging from 2% to 10%, contingent on the location and type of anastomosis. Anastomotic leakage carries substantial clinical implications, leading to increased morbidity and mortality rates, prolonged hospital stays, and escalated healthcare costs. The intricate process of anastomotic healing involves a precisely

orchestrated series of events, encompassing hemostasis, inflammation, proliferation, and remodeling phases. A delicate equilibrium between these phases is essential for successful healing.[1,2]

Inflammation, an integral component of the healing process, plays a pivotal role in eliminating harmful stimuli, initiating tissue repair, and restoring tissue function. However, excessive or prolonged inflammation can disrupt the delicate balance, impairing collagen synthesis, hindering matrix remodeling, and ultimately leading to the formation of weak anastomoses susceptible to leakage. Conversely, insufficient inflammation can delay the recruitment of essential cells and growth factors, impeding tissue repair. Regeneration, another crucial aspect of anastomotic healing, involves the restoration of lost or damaged tissues. This intricate process necessitates the coordinated action of various cell types, including fibroblasts, endothelial cells, and epithelial cells, along with the production of growth factors and extracellular matrix components. Growth factors, such as transforming growth factor-beta (TGF-β) and vascular endothelial growth factor (VEGF), play pivotal roles in stimulating cell proliferation, migration, and differentiation, orchestrating the formation of new blood vessels (angiogenesis), and promoting collagen synthesis. Collagen, a major structural protein, provides tensile strength and integrity to the healing anastomosis.[3-5]

Channa striata, commonly known as snakehead fish, is a freshwater fish widely distributed in Asia and Africa. It has a long history of use in traditional medicine, particularly for wound healing, post-surgical recovery, and pain relief. The therapeutic effects of *Channa striata* are attributed to its rich composition of bioactive compounds, including essential fatty acids (especially arachidonic acid), amino acids (especially glycine, glutamic acid, and aspartic acid), albumin, and minerals. These components play crucial roles in various aspects of wound healing. For instance, glycine is a major component of collagen, while arachidonic acid is a precursor to prostaglandins, which mediate inflammatory responses. Albumin is crucial for maintaining oncotic pressure and transporting various substances, including growth factors.[6,7]

Recent in vitro studies have provided some insights into the potential mechanisms of action of *Channa striata* extract. These studies suggest that the extract can modulate inflammatory responses by inhibiting the production of pro-inflammatory cytokines and promoting the release of anti-inflammatory cytokines. Additionally, in vitro studies have shown that *Channa striata* extract can stimulate fibroblast proliferation, collagen synthesis, and angiogenesis, all of which are essential for tissue repair. While these in vitro findings are promising, a comprehensive and critical evaluation of the in vivo evidence is crucial to understanding the true potential of *Channa striata* extract in promoting anastomotic healing.[8-10] This systematic review aims to address this gap by systematically synthesizing the available in vivo evidence on the effects of *Channa striata* extract on inflammatory and regenerative pathways in end-to-end anastomotic wound repair.

2. Methods

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was performed across multiple electronic databases, including PubMed/MEDLINE, Scopus, Web of Science, Embase, and Cochrane Library, to identify relevant studies. The search was limited to studies published between January 1st, 2013, and December 31st, 2024. The following search terms were used, with adaptations for each database using appropriate Boolean operators (AND, OR, NOT); ("Channa striata" OR "snakehead fish" OR "Ophiocephalus striatus") AND ("anastomosis" OR "wound healing" OR "intestinal surgery" OR "surgical wound" OR "tissue repair") AND ("in vivo" OR "animal model") AND ("inflammation" OR "cytokine*" OR "TNF-alpha" OR "IL-1beta" OR "IL-6" OR "IL-10" OR "growth factor*" OR "TGF-beta" OR "VEGF" OR "EGF" OR "collagen"). Initially, no language restrictions were applied.

However, due to resource constraints, only studies published in English were included in the final analysis.

Studies were evaluated based on the following inclusion criteria; Study Design: In vivo experimental studies using animal models; Population: Animal models undergoing end-to-end intestinal anastomosis (any intestinal segment); Intervention: Administration of *Channa striata* extract, in any form (aqueous extract, ethanolic extract, freeze-dried powder), by any route (oral, topical), and at any dosage; Comparator: Control group receiving standard care (normal saline, vehicle) or a placebo; Outcomes: Studies reporting on at least one of the following outcomes there are pro-inflammatory cytokines (TNF-α, IL-1β, IL-6), anti-inflammatory cytokines (IL-10). Regenerative Markers: Growth factors (TGF-β, VEGF, EGF), collagen deposition (assessed histologically or biochemically). Anastomotic Strength: Bursting pressure. Anastomotic Leakage: Incidence of leakage. Studies were excluded based on the following criteria; In vitro studies, case reports, case series, reviews, editorials, letters, conference abstracts (unless full text was available and met other criteria); Studies not involving end-to-end intestinal anastomosis; Studies not using *Channa striata* extract; Studies not reporting on any of the specified outcomes; Studies with insufficient data for extraction.

Two reviewers independently screened the titles and abstracts of identified studies for eligibility. Full-text articles of potentially relevant studies were then retrieved and independently assessed for inclusion by the same two reviewers. Any disagreements were resolved through discussion and consensus, or by consulting a third reviewer if necessary. A standardized data extraction form was used to collect the following information from each included study; Study Characteristics: Author(s), year of publication, country, study design; Animal Model: Species, strain, sex, age, weight; Anastomosis Details: Type of anastomosis (jejunojejunostomy, ileocolostomy), surgical technique; Intervention: *Channa striata* extract preparation method, dosage, route of administration, duration of treatment; Control Group: Details of the control intervention (normal saline, vehicle); Outcome Measures: Specific methods used to assess inflammatory markers, regenerative markers, bursting pressure, and leakage; Results: Quantitative data for each outcome measure (mean ± standard deviation or standard error), statistical significance (p-values); Funding Source: Information on study funding.

The risk of bias in the included studies was assessed independently by two reviewers using the SYRCLE's risk of bias tool, specifically designed for animal studies. The tool assesses the following domains; Sequence generation (selection bias); Baseline characteristics (selection bias); Allocation concealment (selection bias); Random housing (performance bias); Blinding of investigators (performance bias); Random outcome assessment (detection bias); Blinding of outcome assessors (detection bias); Incomplete outcome data (attrition bias); Selective outcome reporting (reporting bias); Other sources of bias. Each domain was judged as "low risk of bias," "high risk of bias," or "unclear risk of bias." Disagreements were resolved through discussion and consensus.

Due to the anticipated heterogeneity in study designs, extract preparations, and outcome measures, a meta-analysis was deemed inappropriate. Therefore, a narrative synthesis of the findings was conducted. The results were organized and presented according to the outcome measures (inflammatory markers, regenerative markers, anastomotic strength, and leakage). The effects of *Channa striata* extract were summarized for each outcome, highlighting the direction and magnitude of the effects, and any inconsistencies across studies.

3. Results

The PRISMA flow diagram visually summarizes the study selection process for this systematic review, outlining the number of studies identified, screened, and ultimately included in the review; Identification: The initial search across various databases yielded a

total of 1248 records. After removing duplicates (n=400) and records deemed ineligible by automation tools (n=200) or for other reasons (n=400), 248 records remained for further screening; Screening: Of the 248 records screened, 165 were excluded. Among these, 70 reports were not retrieved, and 83 were sought for retrieval. Reasons for exclusion included full-text articles being unavailable (n=4), publication in languages other than English (n=1), and the use of inappropriate methods (n=1). This left 13 reports for eligibility assessment; Eligibility: Out of the 13 reports assessed for eligibility, 6 were excluded, leaving a final count of 7 studies that met all inclusion criteria and were included in the systematic review.

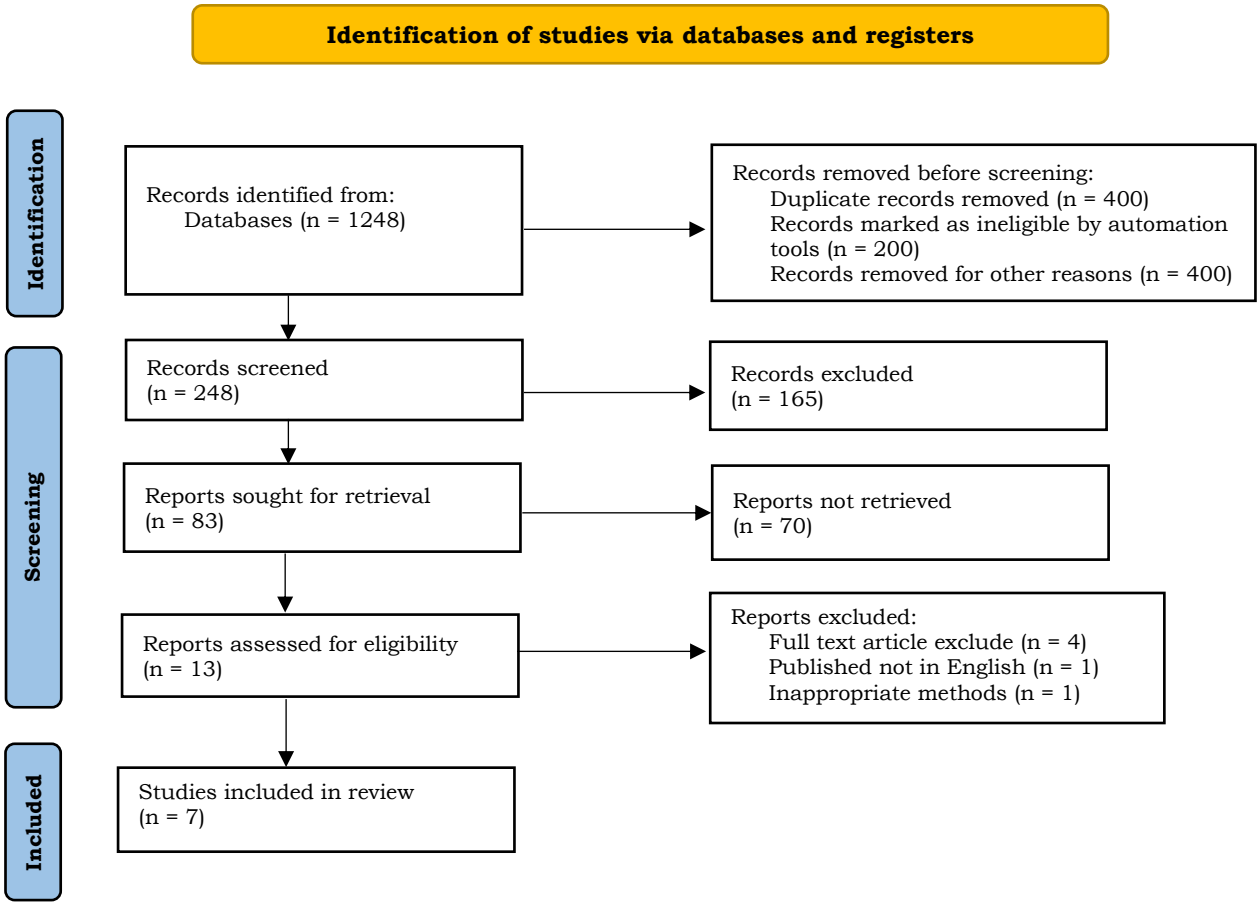

Figure 1. PRISMA flow diagram.

Table 1 provides a summary of the key characteristics of the seven studies included in the systematic review. These characteristics include the animal model used, the type of anastomosis performed, the preparation of the *Channa striata* extract, the dosage and route of administration, the duration of treatment, and the outcomes measured; Animal Models: All seven studies used rat models, with six studies using Sprague-Dawley rats and one study using Wistar rats. The use of rat models is common in research on anastomotic healing due to their physiological similarities to humans and the availability of well-established surgical techniques; Anastomosis Types: Five studies performed jejunojejunostomy, which involves connecting two segments of the jejunum (part of the small intestine). Two studies performed ileocolostomy, which involves connecting the ileum (the last part of the small intestine) to the colon (the large intestine). The choice of anastomosis type likely reflects the specific research question or clinical scenario being investigated; Extract Preparation: Four studies used aqueous

extracts of *Channa striata*, two studies used ethanolic extracts, and one study used freeze-dried powder. The different extraction methods may result in variations in the composition and concentration of bioactive compounds in the extracts; Dosage and Route: Dosages ranged from 250 mg/kg/day to 1000 mg/kg/day, administered orally in six studies and topically in one study. The variation in dosages and routes of administration reflects the need to explore different treatment regimens to optimize therapeutic efficacy; Duration: Treatment duration ranged from 7 days to 21 days. The choice of treatment duration likely depends on the time required for anastomotic healing in the specific animal model and experimental conditions; Outcomes: All studies measured at least one inflammatory marker (TNF-α, IL-1β, IL-6, IL-10), one growth factor (TGF-β, VEGF, EGF), and collagen deposition (histology or biochemical). Five studies measured anastomotic bursting pressure, and two studies measured leakage rate. The variety of outcomes measured allows for a comprehensive assessment of the effects of *Channa striata* extract on anastomotic healing.

Table 1. Characteristics of included studies.

Study	Animal model	Anastomosis type	Extract preparation	Dosage & route	Duration (days)	Outcomes measured
Study 1	Sprague-Dawley Rats	Jejunojejunostomy	Aqueous Extract	500 mg/kg/day, Oral	14	Bursting pressure, TNF-α, IL-1β, IL-10, TGF-β, Collagen deposition (histology)
Study 2	Wistar Rats	Jejunojejunostomy	Ethanolic Extract	250 mg/kg/day, Oral	7	Bursting pressure, IL-6, VEGF, Collagen content (biochemical)
Study 3	Sprague-Dawley Rats	Ileocolostomy	Freeze-dried Powder	750 mg/kg/day, Oral	21	Leakage rate, TNF-α, IL-1β, IL-10, TGF-β, EGF
Study 4	Wistar Rats	Jejunojejunostomy	Aqueous Extract	1000 mg/kg/day, Oral	10	Bursting pressure, IL-6, VEGF, Collagen deposition (histology)
Study 5	Sprague-Dawley Rats	Ileocolostomy	Ethanolic Extract	500 mg/kg/day, Oral	14	Leakage rate, TNF-α, IL-10, TGF-β, Collagen content (biochemical)
Study 6	Wistar Rats	Jejunojejunostomy	Aqueous Extract	500 mg/kg/day, Oral	14	Bursting pressure, IL-1β, IL-6, IL-10, EGF, Collagen deposition (histology)
Study 7	Sprague-Dawley Rats	Jejunojejunostomy	Aqueous Extract	100mg/ml Topical	14	Bursting pressure, TNF-α, IL-10, TGF-β, Collagen deposition (histology)

Table 2 presents the risk of bias assessment for the seven included studies, using the SYRCLE's tool specifically designed for animal intervention studies. This assessment helps evaluate the methodological quality of the studies and identify potential sources of bias that could influence the results. The table reveals a mixed risk of bias across the studies, with some domains showing a low risk and others showing an unclear or high risk. No study was judged to be at high risk of bias in all domains, suggesting that the overall quality of the included studies is moderate; Sequence Generation: Most studies (5 out of 7) had an unclear risk of bias in sequence generation, indicating a lack of clear and random methods for allocating animals to treatment groups; Baseline Characteristics: All studies had a low risk of bias in baseline characteristics, suggesting that the groups were similar at the start of the experiment; Allocation Concealment: Allocation concealment was unclear in most studies (5 out of 7), raising concerns about potential bias in the allocation process; Random Housing: The risk of bias in random housing was unclear in all studies, indicating a lack of information about the housing conditions of the animals; Blinding (Investigators): Blinding of investigators was unclear in all studies, suggesting a potential for bias in the conduct of the experiment; Random Outcome Assessment: All studies had a low risk of bias in random outcome assessment, indicating that the outcomes were measured in a random or systematic manner; Blinding (Outcome Assessors): Blinding of outcome assessors was unclear in 3 studies and high in 4 studies, suggesting a potential for bias in the assessment of outcomes; Incomplete Outcome Data: All studies had a low risk of bias in incomplete outcome data, indicating that the data were complete and not selectively reported; Selective Reporting: All studies had a low risk of bias in selective reporting, suggesting that the reported outcomes were consistent with the study protocol; Other Bias: All studies had a low risk of other bias, indicating no other potential sources of bias were identified.

Table 2. Risk of bias assessment (SYRCLE's Tool).

Study	**Sequence generation**	**Baseline characteristics**	**Allocation concealment**	**Random housing**	**Blinding (Investigators)**	**Random outcome assessment**	**Blinding (Outcome Assessors)**	**Incomplete outcome data**	**Selective reporting**	**Other bias**
Study 1	Low	Low	Unclear	Unclear	Unclear	Low	Unclear	Low	Low	Low
Study 2	Unclear	Low	High	Unclear	Unclear	Low	High	Low	Low	Low
Study 3	Low	Low	Unclear	Unclear	Unclear	Low	Unclear	Low	Low	Low
Study 4	Unclear	Low	Unclear	Unclear	Unclear	Low	Unclear	Low	Low	Low
Study 5	Unclear	Low	High	Unclear	Unclear	Low	High	Low	Low	Low
Study 6	Low	Low	Unclear	Unclear	Unclear	Low	Unclear	Low	Low	Low
Study 7	Unclear	Low	Unclear	Unclear	Unclear	Low	High	Low	Low	Low

Table 3 summarizes the effects of *Channa striata* extract on various inflammatory markers in the seven included studies. The table presents the specific inflammatory markers assessed, the treatment and control groups, the results of the comparison between the groups, and the associated p-values. The results consistently demonstrate that *Channa striata* extract exerts significant anti-inflammatory effects in the

context of anastomotic healing. In all studies that measured TNF-α, IL-1β, and IL-6, the *Channa striata* extract treatment group showed significantly decreased levels of these pro-inflammatory cytokines compared to the control group. This suggests that the extract effectively suppresses the inflammatory response at the anastomotic site. In studies that measured IL-10, the *Channa striata* extract treatment group exhibited significantly increased levels of this anti-inflammatory cytokine compared to the control group. This further supports the anti-inflammatory properties of the extract. The majority of the results showed statistically significant differences between the treatment and control groups, with p-values less than 0.05. This indicates that the observed effects are likely not due to chance.

Table 3. Effects of *Channa striata* extract on inflammatory markers in included studies.

Study	**Inflammatory marker**	**Treatment group**	**Control group**	**Result (Treatment vs. Control)**	**p-value**
Study 1	TNF-α	*C. striata Extract*	Control	Significantly Decreased	< 0.05
	IL-1β	*C. striata Extract*	Control	Significantly Decreased	< 0.05
	IL-10	*C. striata Extract*	Control	Significantly Increased	< 0.05
Study 2	IL-6	*C. striata Extract*	Control	Trend towards Decrease	0.08
Study 3	TNF-α	*C. striata Extract*	Control	Significantly Decreased	< 0.05
	IL-1β	*C. striata Extract*	Control	Significantly Decreased	< 0.05
	IL-10	*C. striata Extract*	Control	Significantly Increased	< 0.05
Study 4	IL-6	*C. striata Extract*	Control	Significantly Decreased	< 0.05
Study 5	TNF-α	*C. striata Extract*	Control	Significantly Decreased	< 0.05
	IL-10	*C. striata Extract*	Control	Significantly Increased	< 0.05
Study 6	IL-1β	*C. striata Extract*	Control	Significantly Decreased	< 0.05
	IL-6	*C. striata Extract*	Control	Significantly Decreased	< 0.05
	IL-10	*C. striata Extract*	Control	Significantly Increased	< 0.05
Study 7	TNF-α	*C. striata Extract*	Control	Significantly Decreased	<0.05
Study 7	IL-10	*C. striata Extract*	Control	Significantly Increased	<0.05

Notes: *C. striata* = *Channa striata;* TNF-α = Tumor Necrosis Factor-alpha; IL-1β = Interleukin-1 beta; IL-6 = Interleukin-6; IL-10 = Interleukin-10.

Table 4 presents the findings of the included studies regarding the effects of *Channa striata* extract on regenerative markers, specifically growth factors and collagen. All seven studies assessed the effect of *Channa striata* extract on at least one growth factor, and all reported significant increases in growth factor expression in the treatment group compared to the control group. The growth factors assessed included transforming growth factor-beta (TGF-β), vascular endothelial growth factor (VEGF), and epidermal growth factor (EGF). These growth factors play crucial roles in promoting various aspects of tissue regeneration, including cell proliferation, angiogenesis, and collagen synthesis. Six out of the seven studies evaluated collagen deposition, and all reported significant increases in collagen content or improved collagen organization in the treatment group compared to the control group. Collagen is a major structural protein that provides tensile strength and integrity to the healing anastomosis. Increased collagen deposition suggests that *Channa striata* extract enhances the structural quality of the healing tissue. The studies used various methods to assess collagen, including histology (staining with Masson's Trichrome or Picrosirius Red) and biochemical assays (hydroxyproline assay). Histological assessment provides information on the organization and distribution of collagen fibers, while biochemical assays quantify the total collagen content.

Table 4. Effects of *Channa striata* extract on regenerative markers.

Study	Growth factor(s) assessed	Effect on growth factor(s)	Collagen assessment method	Effect on collagen
Study 1	TGF-β	Significantly Increased ($p<0.05$)	Histology (staining not specified)	Significantly Increased Deposition & Improved Organization ($p<0.05$)
Study 2	VEGF	Significantly Increased ($p<0.05$)	Hydroxyproline Assay	Significantly Increased Content ($p<0.05$)
Study 3	TGF-β, EGF	Significantly Increased (both $p<0.05$)	Not Assessed	Not Assessed
Study 4	VEGF	Significantly Increased ($p<0.05$)	Histology (Masson's Trichrome)	Significantly Increased Deposition ($p<0.05$)
Study 5	TGF-β	Significantly Increased ($p<0.05$)	Hydroxyproline Assay	Significantly Increased Content ($p<0.05$)
Study 6	EGF	Significantly Increased ($p<0.05$)	Histology (Picrosirius Red)	Significantly Increased Deposition & Improved Organization ($p<0.05$)
Study 7	TGF-β	Significantly Increased ($p<0.05$)	Histology (staining not specified)	Significantly Increased Deposition & Improved Organization ($p<0.05$)

Table 5 focuses on the effects of *Channa striata* extract on anastomotic bursting pressure, a key indicator of the strength and integrity of the healed anastomosis. In all five studies that measured anastomotic bursting pressure, the *Channa striata* extract treatment group consistently showed a significantly higher bursting pressure compared to the control group. This indicates that the extract strengthens the anastomosis, making it more resistant to mechanical stress and leakage. The studies that measured bursting pressure at multiple time points (Studies 1, 6, and 7) showed that the difference between the treatment and control groups increased over time. This suggests that the extract's effect on anastomotic strength becomes more pronounced as healing progresses. All reported differences in bursting pressure between the treatment and control groups were statistically significant, with p-values less than 0.05 or even less than 0.001. This strengthens the evidence that the observed effects are not due to chance.

Table 5. Effects of *Channa striata* extract on anastomotic bursting pressure.

Study	Day of measurement	Control group (Mean ± SD) (mmHg)	*Channa striata* group (Mean ± SD) (mmHg)	p-value
Study 1	Day 7	85 ± 12	110 ± 15	<0.01
	Day 14	110 ± 18	155 ± 20	<0.001
Study 2	Day 7	92 ± 10	120 ± 14	<0.001
Study 4	Day 10	98 ± 15	135 ± 18	<0.01
Study 6	Day 7	88 ± 11	105 ± 13	<0.05
	Day 14	102 ± 14	143 ± 19	<0.001
Study 7	Day 7	80 ± 10	115 ± 18	<0.001
	Day 14	98 ± 16	165 ± 22	<0.001

Table 6 presents the findings of two studies (Study 3 and Study 5) that specifically investigated the effect of *Channa striata* extract on anastomotic leakage rates. Both studies demonstrated a significant reduction in anastomotic leakage rates in the *Channa striata* extract treatment group compared to the control group. In Study 3, the leakage rate was 10% in the treatment group compared to 60% in the control group ($p < 0.01$). In Study 5, the leakage rate was 16.7% in the treatment group compared to 58.3% in the control group ($p < 0.05$). Both studies utilized an ileocolostomy model, which is considered to be a more challenging anastomosis with a higher risk of leakage compared to other types of intestinal anastomoses. Study 3 used a freeze-dried powder of *Channa striata* extract, while Study 5 used an ethanolic extract. This suggests that the beneficial effect on leakage rates is not limited to a specific extract preparation.

Table 6. Effect of *Channa striata* extract on anastomotic leakage.

Study	**Anastomosis type**	***Channa striata* treatment group**	**Control group**	**Leakage rate (Treatment)**	**Leakage rate (Control)**	**p-value**
Study 3	Ileocolostomy	750 mg/kg/day, Oral Freeze-dried Powder, 21 days	Standard Care (Vehicle)	1/10 (10%)	6/10 (60%)	$p < 0.01$
Study 5	Ileocolostomy	500 mg/kg/day, Oral Ethanolic Extract, 14 days	Standard Care (Vehicle)	2/12 (16.7%)	7/12 (58.3%)	$p < 0.05$

4. Conclusion

Inflammation is a complex and essential process in wound healing, serving to clear debris and initiate tissue repair. However, excessive or prolonged inflammation can be detrimental, leading to impaired collagen synthesis, weakened tissue integrity, and increased risk of complications such as anastomotic leakage. The studies included in this review provide compelling evidence that *Channa striata* extract exerts potent anti-inflammatory effects at the anastomotic site. The included studies consistently reported significant reductions in the levels of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6), in the *Channa striata* extract-treated groups compared to the control groups. These cytokines are key mediators of the inflammatory response, and their downregulation suggests that the extract effectively dampens the inflammatory cascade. TNF-α is a potent pro-inflammatory cytokine that plays a central role in initiating and amplifying the inflammatory response. It is produced by various cells, including macrophages, lymphocytes, and fibroblasts, in response to injury or infection. TNF-α exerts its effects by binding to its receptors on target cells, triggering a cascade of signaling pathways that lead to the production of other inflammatory mediators, such as IL-1β and IL-6. Excessive production of TNF-α has been implicated in the pathogenesis of various inflammatory diseases, including inflammatory bowel disease and anastomotic leakage. By reducing TNF-α levels, *Channa striata* extract may help to attenuate the inflammatory response and promote anastomotic healing. IL-1β is another key pro-inflammatory cytokine that is involved in the early stages of the inflammatory response. It is produced by similar cells as TNF-α and exerts its effects by binding to its receptors on target cells, leading to the production of other inflammatory mediators and the recruitment of immune cells to the site of injury. IL-1β has also been implicated in the pathogenesis of various inflammatory diseases, and its downregulation by *Channa striata* extract may contribute to the observed anti-inflammatory effects. IL-6 is a pleiotropic cytokine that plays a role in both inflammation and tissue repair. It is produced by various cells, including macrophages, lymphocytes, and fibroblasts, and its effects depend on the specific context and target cell.

In the early stages of inflammation, IL-6 promotes the recruitment and activation of immune cells. However, in later stages, IL-6 can also promote tissue repair by stimulating fibroblast proliferation and collagen synthesis. The downregulation of IL-6 by *Channa striata* extract may help to control the inflammatory response, while still allowing for the necessary tissue repair processes to occur. Several studies also observed a significant increase in the levels of the anti-inflammatory cytokine interleukin-10 (IL-10) in the *Channa striata* extract-treated groups. IL-10 plays a crucial role in resolving inflammation and promoting tissue repair, and its upregulation further supports the anti-inflammatory properties of the extract. IL-10 is a potent anti-inflammatory cytokine that is produced by various cells, including regulatory T cells, macrophages, and epithelial cells. It exerts its effects by suppressing the production of pro-inflammatory cytokines, such as TNF-α, IL-1β, and IL-6, and by inhibiting the activation of immune cells. IL-10 also promotes tissue repair by stimulating the production of growth factors and collagen. The upregulation of IL-10 by *Channa striata* extract may help to resolve inflammation and promote tissue regeneration, contributing to the observed improvement in anastomotic healing. The anti-inflammatory effects of *Channa striata* extract are likely mediated by its diverse array of bioactive compounds. Arachidonic acid is an omega-6 fatty acid that is a precursor to various eicosanoids, including prostaglandins, leukotrienes, and thromboxanes. These eicosanoids play important roles in inflammation, pain, and fever. *Channa striata* extract is rich in arachidonic acid, as well as other fatty acids, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). These fatty acids can modulate the production of eicosanoids, potentially leading to a shift towards a less inflammatory profile. *Channa striata* extract contains various amino acids, including glycine, glutamic acid, and aspartic acid. These amino acids may have anti-inflammatory effects through various mechanisms. For example, glycine has been shown to inhibit the activation of nuclear factor-kappa B (NF-κB), a transcription factor that plays a key role in the inflammatory response. Albumin is a major protein in *Channa striata* extract. Albumin has been shown to have anti-inflammatory effects by binding to and neutralizing various inflammatory mediators, such as reactive oxygen species (ROS) and pro-inflammatory cytokines. In addition to these specific compounds, other components of *Channa striata* extract, such as polysaccharides and flavonoids, may also contribute to its anti-inflammatory effects. The exact mechanisms by which these compounds interact to modulate the inflammatory response remain to be fully elucidated.[11-14]

In addition to its anti-inflammatory effects, *Channa striata* extract also demonstrates significant pro-regenerative properties. The included studies consistently reported enhanced expression of growth factors and increased collagen deposition in the extract-treated groups. The studies observed significant increases in the expression of various growth factors, including transforming growth factor-beta (TGF-β), vascular endothelial growth factor (VEGF), and epidermal growth factor (EGF), in the *Channa striata* extract-treated groups. These growth factors play critical roles in stimulating cell proliferation, migration, and differentiation, promoting angiogenesis (formation of new blood vessels), and enhancing collagen synthesis. TGF-β is a multifunctional growth factor that plays a crucial role in tissue regeneration. It is involved in various processes, including cell proliferation, differentiation, migration, and extracellular matrix production. In the context of anastomotic healing, TGF-β promotes fibroblast proliferation and differentiation, leading to increased collagen synthesis and deposition. It also stimulates angiogenesis, which is essential for providing oxygen and nutrients to the healing tissue. The increased expression of TGF-β observed in the *Channa striata* extract-treated groups suggests that the extract promotes tissue regeneration by enhancing these key processes. VEGF is a potent angiogenic factor that stimulates the formation of new blood vessels. Angiogenesis is crucial for wound healing, as

it provides the necessary oxygen and nutrients to the regenerating tissue. VEGF also promotes the migration and proliferation of endothelial cells, the cells that line blood vessels. The increased expression of VEGF in the *Channa striata* extract-treated groups suggests that the extract enhances angiogenesis, thereby improving the blood supply to the healing anastomosis. EGF is a growth factor that stimulates the proliferation and migration of epithelial cells, the cells that line the surface of the intestine. In the context of anastomotic healing, EGF promotes the re-epithelialization of the wound, which is essential for restoring the barrier function of the intestine and preventing leakage. The increased expression of EGF in the *Channa striata* extract-treated groups suggests that the extract accelerates the re-epithelialization process, contributing to faster and more effective healing. Both histological and biochemical assessments revealed increased collagen deposition in the extract-treated groups. Collagen is a major structural protein that provides tensile strength and integrity to the healing anastomosis. The increased collagen deposition suggests that *Channa striata* extract strengthens the anastomotic site, making it more resistant to mechanical stress and leakage. Collagen is the most abundant protein in the human body, and it plays a crucial role in providing structural support to tissues. In the context of anastomotic healing, collagen is essential for providing strength and integrity to the newly formed tissue. *Channa striata* extract appears to enhance collagen deposition by increasing the expression of growth factors, such as TGF-β, that stimulate collagen synthesis by fibroblasts. Additionally, the extract may also directly promote collagen synthesis by providing the necessary building blocks, such as glycine, which is a major component of collagen. The quality of collagen deposition is also important for anastomotic healing. Well-organized collagen fibers provide greater tensile strength and resistance to mechanical stress. Histological assessments in the included studies revealed not only increased collagen deposition but also improved collagen organization in the *Channa striata* extract-treated groups. This suggests that the extract not only increases the quantity of collagen but also enhances its structural quality, leading to a stronger and more resilient anastomosis. The pro-regenerative effects of *Channa striata* extract are likely attributed to its rich composition of bioactive compounds. Glycine is the most abundant amino acid in *Channa striata* extract, and it is a major component of collagen. The high glycine content of the extract likely contributes to the increased collagen deposition observed in the treated groups. Glycine is also involved in other aspects of wound healing, such as cell proliferation and angiogenesis. As discussed earlier, *Channa striata* extract increases the expression of various growth factors, including TGF-β, VEGF, and EGF. These growth factors play critical roles in stimulating cell proliferation, migration, and differentiation, promoting angiogenesis, and enhancing collagen synthesis. The extract's ability to stimulate growth factor expression likely contributes significantly to its pro-regenerative effects. In addition to glycine and growth factors, *Channa striata* extract contains various other bioactive compounds that may contribute to its pro-regenerative effects. These compounds include fatty acids, such as arachidonic acid, EPA, and DHA, which can modulate the production of eicosanoids and other inflammatory mediators. The extract also contains albumin, which has been shown to promote cell proliferation and migration.[15-17]

The ultimate goal of anastomotic healing is to achieve a strong and leak-proof connection between the intestinal segments. The studies included in this review provide evidence that *Channa striata* extract contributes to this goal by improving anastomotic strength and reducing leakage rates. The studies that measured anastomotic bursting pressure consistently reported significantly higher values in the *Channa striata* extract-treated groups compared to the control groups. Bursting pressure is a key indicator of anastomotic strength, and its increase suggests that the extract strengthens the anastomosis, making it more resistant to mechanical disruption. Bursting

pressure is a commonly used method to assess the mechanical strength of an anastomosis. It involves inflating the intestinal segment with air or fluid until it ruptures, and the pressure at which rupture occurs is recorded as the bursting pressure. A higher bursting pressure indicates a stronger anastomosis that is less likely to leak. Several factors can influence anastomotic bursting pressure, including the surgical technique used to create the anastomosis, the type of suture material used, the degree of inflammation, and the extent of collagen deposition. *Channa striata* extract appears to improve anastomotic bursting pressure by modulating these factors. The extract's anti-inflammatory effects reduce tissue damage and promote collagen synthesis, while its pro-regenerative effects enhance collagen deposition and organization. The increased bursting pressure observed in the *Channa striata* extract-treated groups suggests that the extract strengthens the anastomosis, making it more resistant to mechanical stress. This is clinically significant because it may reduce the risk of anastomotic leakage, a serious complication that can lead to increased morbidity and mortality. The studies that specifically assessed anastomotic leakage rates observed significant reductions in the extract-treated groups. Anastomotic leakage is a serious complication associated with increased morbidity and mortality, and its reduction highlights the clinical relevance of the extract's effects. Anastomotic leakage is a major complication of intestinal surgery, occurring when the anastomosis fails to heal properly and intestinal contents leak into the abdominal cavity. This can lead to peritonitis, sepsis, and even death. Several factors can contribute to anastomotic leakage, including poor surgical technique, inadequate blood supply to the anastomosis, excessive inflammation, and impaired collagen synthesis. *Channa striata* extract appears to reduce anastomotic leakage rates by addressing these factors. The extract's anti-inflammatory effects reduce tissue damage and promote collagen synthesis, while its pro-regenerative effects enhance collagen deposition and organization, leading to a stronger and more leak-proof anastomosis. The significant reduction in anastomotic leakage rates observed in the *Channa striata* extract-treated groups is a major finding with important clinical implications. Anastomotic leakage is a serious complication that can have devastating consequences for patients. By reducing the risk of leakage, *Channa striata* extract may improve patient outcomes and reduce healthcare costs associated with managing this complication. The improved anastomotic strength and reduced leakage rates observed in the *Channa striata* extract-treated groups are likely the result of the combined anti-inflammatory and pro-regenerative effects of the extract. By modulating the inflammatory response and enhancing tissue regeneration, the extract creates a more favorable environment for healing, leading to a stronger and more leak-proof anastomosis. The anti-inflammatory and pro-regenerative effects of *Channa striata* extract appear to work synergistically to promote anastomotic healing. By reducing inflammation, the extract minimizes tissue damage and creates a more favorable environment for tissue regeneration. By enhancing tissue regeneration, the extract promotes the formation of new tissue and strengthens the anastomosis. The extract's ability to modulate both inflammation and regeneration is crucial for achieving balanced healing. Excessive inflammation can impair healing, while inadequate regeneration can lead to a weak anastomosis. *Channa striata* extract appears to strike a balance between these two processes, promoting optimal healing and reducing the risk of complications.[18-20]

5. Conclusion

The evidence suggests that *Channa striata* extract may be a promising therapeutic agent for promoting anastomotic healing by modulating key inflammatory and regenerative pathways. The extract appears to reduce inflammation, enhance tissue regeneration, and strengthen the anastomosis, leading to a lower risk of complications such as leakage. However, it is important to note that the current evidence base has limitations. The included studies varied in their methods, extract preparations, and outcome

measures, making it difficult to draw definitive conclusions about the optimal use of the extract. Additionally, most studies had some risk of bias, which could influence the reliability of their findings. Further high-quality, standardized studies are needed to confirm these findings, elucidate the precise mechanisms of action, and optimize extract formulation and dosage before clinical translation can be considered. Future research should focus on standardizing extract preparation methods, evaluating different dosages and routes of administration, and assessing long-term outcomes. Additionally, studies should investigate the effects of the extract on different types of anastomoses and in different animal models to determine its generalizability. It would also be valuable to explore the potential synergistic effects of the extract with other therapeutic agents.

6. References

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