INPLASY

Systematic review of the mechanisms of traditional polyherbal medicine in treatment and prevention of colorectal cancer

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ADMINISTRATIVE INFORMATION

INTRODUCTION

Review question / Objective What are the mechanisms of traditional polyherbal medicine in the treatment and prevention of colorectal cancer.

Rationale Colorectal cancer is a malignancy of the colon or rectum that starts as a benign adenomatous polyp and slowly develops into a precancerous lesion and later becomes a carcinoma (Kuipers et al., 2015; Dekker et al., 2019; Keum et al., 2020). It continues to pose a significant global health burden as the third most common cancer, with over 1.9 million cases worldwide in 2020, while increasing mortality rates. (Sung et al., 2021). Although improvements in screening and treatment advances have been made, the prevalence is estimated to grow to 3.2 million by 2040, with variations in outcomes in different geographic regions (Malla et al., 2022; Sung et al., 2021). Current treatments mainly focus on surgery, together with chemotherapy and radiotherapy. Other treatments, such as targeted therapy and immunotherapy, are also used in specific cases. Yet, these conventional approaches face significant limitations and side effects (Fahlahllah et al., 2024).

Traditional polyherbal medicine, especially in Asian countries, has been used with conventional therapy as a complementary or alternative medicine to treat various diseases, including cancer. These formulations contain multiple ingredients and work through multiple pathways and mechanisms rather than acting on one target, resulting in an inescapable tumor (Chen et al., 2023; Wei et al., 2023). Recent preclinical research also proves that some polyherbal compounds may induce apoptosis, anti-proliferation, and anti-angiogenesis, and regulate gut microbiome (Tian et al., 2020). Much preclinical and clinical trial research shows that Traditional Chinese Medicine

slows tumor growth, reduces metastasis, reverses chemotherapy resistance, reduces inflammation, improves the effectiveness of conventional therapies, and reduces side effects (Chen et al., 2023). One decoction, Pien Tze Huang, is known to have a chemopreventive effect in vivo model by altering gut microbiota and blocking inflammatory signaling pathways (Chen et al., 2017). The Astragali Radix-Curcumae Rhizoma combination is known to reduce cancer stem cell properties by modulating the Wnt signaling pathway (Gou et al., 2023). Other studies also show that certain polyherbal compounds might also enhance the effectiveness of chemotherapy drugs, resulting in the potential use of lower doses and lower toxicity (Yang et al., 2025).

However, despite these findings from preclinical and clinical studies, there is still a significant gap remaining in understanding how the traditional polyherbal compound mechanisms work and whether they really benefit carcinoma patients. There may be considerable inconsistency due to how these polyherbal decoctions are formulated, prepared, and tested in different studies, making it difficult to draw a summarized conclusion or compare the results (Tang et al., 2024). With these facts, it is a challenge to standardize the preparations to ensure the quality of traditional polyherbal medicines, questioning the optimal dosing and potential interaction with conventional treatments, and long-term safety remains largely unknown. (Sujithra et al., 2025). Therefore, a systematic review is evaluated by using existing literature to determine what we really know about polyherbal medicine in the treatment and prevention of colorectal cancer and identify the promising formulation and mechanism worth further investigation. This highlights the critical research gaps that must be addressed before the traditional remedies are integrated into the treatment and therapy in modern cancer care.

Condition being studied Colorectal cancer is a malignancy of the colon or rectum that starts as a benign adenomatous polyp and slowly develops into a precancerous lesion and later becomes a carcinoma (Kuipers et al., 2015; Dekker et al., 2019; Keum et al., 2020). It continues to pose a significant global health burden as the third most common cancer, with over 1.9 million cases worldwide in 2020, while increasing mortality rates. (Sung et al., 2021). Although improvements in screening and treatment advances have been made, the prevalence is estimated to grow to 3.2 million by 2040, with variations in outcomes in different geographic regions (Malla et al., 2022; Sung et al., 2021). Current treatments mainly focus on surgery, together with chemotherapy and radiotherapy. Other treatments, such as targeted therapy and immunotherapy, are also used in specific cases. Yet, these conventional approaches face significant limitations and side effects (Fahlahllah et al., 2024).

METHODS

Search strategy A comprehensive search was performed across four electronic databases, PubMed, SCOPUS, AMED, and LILACS, using predefined keyword combinations targeting polyherbal formulations, colorectal cancer, and mechanistic investigations.

Participant or population CRC-induced rodent models .

Intervention Traditional polyherbal formulations.

Comparator Vehicle/control, untreated, standard preventive agent, chemotherapy alone, placebo.

Study designs to be included in vivo.

Eligibility criteria The research question for this systematic review was "What are the mechanisms of action of traditional polyherbal formulations in preventing and treating colorectal cancer?" A global database that prospectively tracks systematic reviews in health and social care, along with their PICO elements (Population, Intervention, Comparator, and Outcomes), as shown in Table 2, served as the foundation for the inclusion and exclusion criteria. The researcher assessed the eligibility requirement independently. The titles and abstracts serve as the basis for the preliminary assessment. This systematic review includes articles published in English with full texts and excludes duplicate papers. Human and in vitro studies, editorials, case reports, dissertations, theses, reports, and any papers not relevant to the primary issues were also excluded.

Information sources A comprehensive search of online databases was performed by the researcher. The databases searched were the U.S. National Library of Medicine and National Institutes of Health (PubMed) (link: https://pubmed.ncbi.nlm.nih.gov/) (accessed 28 September, 2025), SCOPUS (https://www.scopus.com/sources) (accessed 28 September, 2025), the Allied and Complementary Medicine Database (AMED) (https://research.ebsco.com/c/ozixw7/search) (accessed 28 September, 2025), and the Latin American and Caribbean Health Sciences Literature (LILACS)

(https://lilacs.bvsalud.org/en/home-en-2/) (accessed 28 September, 2025). The search included studies published from 2015 up to September 2025.

Main outcome(s) A systematic review is evaluated by using existing literature to determine what we really know about polyherbal medicine in the treatment and prevention of colorectal cancer and identify the promising formulation and mechanism worth further investigation.

Additional outcome(s) This highlights the critical research gaps that must be addressed before the traditional remedies are integrated into the treatment and therapy in modern cancer care.

Data management The researcher screened all abstracts and titles, including the article if it met the criteria: mechanisms of traditional polyherbal medicine in the treatment and prevention of colorectal cancer. The researcher then extracted data from the included studies and entered it into Google Sheets. The data were abstracted using a standardized form of the key study format, including the first author's name, publication year, the author's publication country, rodent model, age, sex, sample sizes, disease-inducing method, herbal compound name, experimental group, treatment compounds, dosage, method of admission, duration of study, ingredient of polyherbal medicine, known active compounds, mechanism of pathway, effect of mechanism, and results of the finding. To enhance the results of these visual representations, the data were presented in figures and tables using Google Colab (https://colab.research.google.com).

Quality assessment / Risk of bias analysis To check for risk of bias, the researcher, B.B.L., used a checklist from the Systematic Review Centre for Laboratory Animal Experimentation (SYRCLE). This tool, based on the Cochrane Collaboration's Risk of Bias Tool, has ten items in six primary areas: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other sources of bias. Each area was rated as "Yes" (low risk), "No" (high risk), or "NC" (not clear due to insufficient information). A point was given for each "Yes" answer.
The researchers, B.B.L. and W.P.L., rated each study's risk of bias as "low," "unclear," or "high" in areas such as sequence generation, baseline characteristics, allocation concealment (selection bias), random housing and blinding (performance bias), random outcome assessment and blinding (detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias), and other possible sources of bias. After finishing the assessments, the reviewers, S.A. and S.C., compared and discussed the results.

Strategy of data synthesis The researchers, B.B.L. and W.P.L., screened all abstracts and titles, including the article if it met the criteria: mechanisms of traditional polyherbal medicine in the treatment and prevention of colorectal cancer. S.A. resolved the conflict by concluding that the study satisfied the inclusion criteria in order to prevent bias. After that, B.B.L. and W.P.L. took data out of the included studies and imported it into Google Sheets. The data were abstracted using a standardized form of the key study format, including the first author's name, publication year, the author's publication country, rodent model, age, sex, sample sizes, disease-inducing method, herbal compound name, experimental group, treatment compounds, dosage, method of admission, duration of study, ingredient of polyherbal medicine, known active compounds, mechanism of pathway, effect of mechanism, and results of the finding. Finally, the data were checked by S.C. to prevent inconsistency and resolved through discussion among the participating researchers. To enhance the results of these visual representations, the data were presented in figures and tables using Google Colab (https://colab.research.google.com).

Subgroup analysis None reported.

Sensitivity analysis None reported.

Language restriction English.

Country(ies) involved Thailand.

Keywords Mechanisms; Polyhebal; colorectal cancer.

Dissemination plans This article aims to share the findings of this systematic review with researchers in the fields of oncology, pharmacology, and traditional medicine. The review's key results summaries of the mechanisms, active compounds, and biological pathways through which traditional polyherbal medicine may contribute to the treatment and prevention of colorectal cancer will be communicated through multiple academic channels. The primary method of dissemination will be publication in a peer-reviewed scientific journal, complemented by presentations at relevant research conferences and seminars. In addition, summaries of the findings will be shared through research networks, institutional platforms, and academic profiles to ensure broad visibility

within the scientific community. Dissemination activities will be carried out by the research team following completion and publication of the review.

Contributions of each author

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