

# Phytochemical and Pharmacological Insights of *Sanguinaria Canadensis* a Narrative Review

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## Abstract

### Background

*Sanguinaria canadensis* (bloodroot) is a medicinal plant belonging to the Papaveraceae family known for its rich content of bioactive isoquinoline alkaloids. Among these, benzophenanthridine alkaloids such as sanguinarine and chelerythrine have been widely studied for their diverse biological activities. Traditionally, the plant has been used for respiratory and dermatological conditions. Recent pharmacological research has highlighted its antimicrobial anti-inflammatory and anticancer properties.

## Objective

This review aims to evaluate the phytochemical constituents and pharmacological properties of *Sanguinaria canadensis*. It focuses on the molecular mechanisms underlying its biological activities, p The review also explores traditional applications and emerging approaches such as network pharmacology. Additionally, it seeks to identify gaps in current research and assess safety concerns associated with its use.

## Methods

A narrative literature review was conducted using databases including PubMed, Scopus, Science Direct, and Google Scholar. Relevant studies published in English were selected using predefined keywords. Experimental and review articles focusing on phytochemistry and pharmacological activity were included.

## Results

*Sanguinaria canadensis* is a medicinal plant enriched with bioactive isoquinoline alkaloids, notably sanguinarine and chelerythrine, which exhibit antimicrobial, anti-inflammatory, and anti-proliferative properties. These effects are mediated through mechanisms such as apoptosis induction, suppression of inflammatory mediators, and modulation of key cellular signaling pathways. Additionally safety concerns including cytotoxicity and lack of standardized dosing, restrict its therapeutic application. Further well-designed clinical and translational studies are essential to establish its efficacy, safety, and potential role in contemporary and integrative medical practice.

## Conclusion

*Sanguinaria canadensis* is a pharmacologically important medicinal plant rich in bioactive isoquinoline alkaloids, particularly sanguinarine and chelerythrine. Experimental evidence suggests that these constituents exhibit antimicrobial, anti-inflammatory, and anti-proliferative activities through mechanisms such as apoptosis induction, inhibition of inflammatory mediators, and modulation of signaling pathways including NF- $\kappa$ B and MAPK. clinical translation remains limited due to safety concerns. In homoeopathy, the drug continues to hold therapeutic relevance, though further scientific validation is required. Future research should focus on bridging the gap between experimental pharmacology and clinical application.

## Keywords

*Sanguinaria canadensis*, sanguinarine, phytochemistry, antimicrobial, apoptosis, alkaloids, pharmacology, Network pharmacology

## 1. Introduction

Sanguinarine is a naturally occurring alkaloid present in various medicinal plants, known for its wide range of biological activities, including the modulation of nuclear factor-kappa B and several enzymatic processes.(1) Sanguinarine is a benzophenanthridine alkaloid obtained from the rhizomes of the plant *Sanguinaria canadensis*. It exists in two forms: a cationic iminium form and a neutral alkanolamine form. Among these, only the iminium form has the ability to intercalate effectively with DNA and RNA. However, both forms are capable of interacting with important biological proteins such as serum albumins, lysozyme, and hemoglobin. Owing to its diverse and significant biological properties, sanguinarine has been the subject of extensive research. Its wide-ranging activities highlight its potential as a promising therapeutic agent, especially in the treatment of chronic diseases such as cancer and asthma.(2) Despite its broad occurrence, there is limited information available on its genetic diversity and population structure. Although the species is relatively common, it has been identified as a species of concern due to its unique reproductive and dispersal strategies, along with increasing exploitation for medicinal use.

### 1.1 Phytochemical Study

Sanguinarine was chosen to further test whether it is potentiation on kanamycin inhibition that exhibits dose dependent synergistic effect. The combination of sanguinarine and various aminoglycosides, including kanamycin, tobramycin, gentamicin, neomycin, amikacin and streptomycin, on bacterial growth was investigated by checkerboard assay with *E. coli* MG1655.(4) It contains eight biologically significant isoquinoline alkaloids, including six quaternary benzophenanthridine alkaloids sanguinarine, chelerythrine, sanguilutine, chelilutine, sanguirubine, and chelirubine—as well as two protopine alkaloids, protopine and allocryptopine. Most studies on these compounds have focused on their anticancer properties, particularly those of sanguinarine and chelerythrine. However, these alkaloids have also been reported to exhibit a range of other biological activities, including antimicrobial, cardiovascular, neuroreceptor-modulating, and anti-inflammatory effects.(5)

## 1.2 Traditional Applications

Despite their pharmacological potential, compounds derived from *S. canadensis* have not yet been successfully developed into effective therapeutic agents. Instead, their use has been linked to various clinical toxicities, including mouthwash-induced leukoplakia, tissue necrosis associated with cancer salves, and instances of treatment failure. This review examines the historical applications of *S. canadensis*, along with the molecular mechanisms of its benzophenanthridine and protopine alkaloids. It also considers the role of natural variation in alkaloid composition as a possible explanation for the inconsistent efficacy and observed toxic effects. Furthermore, current veterinary and medicinal uses of the plant are discussed, alongside an evaluation of the challenges hindering the pharmaceutical development of alkaloid-based therapies derived from *S. canadensis*.(5)

## 2 Antimicrobial, Antinflammatory and Oncologic molecular mechanism

### 2.1 Antimicrobial

Sanguinarine exhibits a wide range of antimicrobial and anti-inflammatory activities. In vitro studies suggest that the antiplaque effect of *Sanguinaria* is primarily attributed to its ability to prevent bacterial adhesion to the newly formed pellicle. Additionally, its concentration within dental plaque is significantly higher—approximately 10 to 100 times greater than in saliva—which further enhances its antimicrobial effectiveness.(6) Extracts of *S. canadensis* were found to exhibit notable antimycobacterial activity specifically against *M. aurum* (MIC = 62.5 µg/ml). Bioassay-guided fractionation of the root extract resulted in the isolation of two well-known benzophenanthridine alkaloids, sanguinarine and chelerythrine.(7)

### 2.2 Ant-inflammatory

#### Anti-inflammatory Properties

*Sanguinaria canadensis* demonstrates notable anti-inflammatory activity, largely attributed to its isoquinoline alkaloids, particularly sanguinarine. Evidence from experimental studies indicates that sanguinarine modulates inflammatory responses by inhibiting key signaling pathways such as nuclear factor kappa B (NF-κB), leading to reduced production of pro-inflammatory cytokines including TNF-α, IL-1β, and IL-6. It has also been associated with suppression of cyclooxygenase-2 (COX-2), thereby decreasing prostaglandin synthesis. Additionally, its role in regulating oxidative stress and reactive oxygen species (ROS) contributes to limiting tissue damage. Modulation of MAPK pathways further supports its anti-inflammatory potential. However, these findings are primarily based on preclinical studies, and clinical validation remains limited.

### 2.2 Oncology

In solid tumors, cancer cells invade surrounding tissues by degrading the basement membrane through proteolytic activity, leading to metastasis—the primary cause of cancer-related deaths. This process is driven by interactions between tumor cells and an inflamed microenvironment, where inflammatory cells release enzymes such as matrix metalloproteinases (MMPs). Increased expression of MMP-2 and

MMP-9 in tumor tissues promotes extracellular matrix degradation and enhances cancer cell migration.(8) The discovery of new cytotoxic compounds effective against resistant cancer cells, such as melanoma, remains a key research priority. In this study, extracts from *Chelidonium majus*, *Mahonia aquifolium*, and *Sanguinaria canadensis*, collected at different growth stages and from various plant parts, were evaluated against FaDu, SCC-25, MCF-7, and MDA-MB-231 cancer cell lines. Most extracts exhibited greater cytotoxicity than the standard anticancer drug etoposide, with the highest activity observed in *Sanguinaria canadensis* extracts obtained prior to flowering.(9) In addition to inducing cell death, *Sanguinaria canadensis* suppresses key tumor-promoting processes such as invasion, angiogenesis, and metastasis across various cancers. It also enhances the efficacy of several chemotherapeutic drugs and demonstrates activity against multiple multidrug-resistant cancer types.(10)

This review summarizes the anticancer effects of berberine, sanguinarine, and chelerythrine against colorectal and gastric cancers. These alkaloids reduce tumor growth, inhibit EMT, modulate key signaling pathways, and induce apoptosis and autophagy. They also enhance the efficacy of standard chemotherapeutic drugs and can restore drug sensitivity in resistant cancers.(11) Our findings suggest that sanguinarine exerts anticancer effects by inhibiting cell proliferation, invasion, and angiogenesis, while promoting apoptosis within tumor sites. However, clinical studies have also indicated that sanguinarine and its related compounds may be associated with precancerous changes in oral and skin tissues.(12)

### **3. Proliferative Mechanism of *Sanguinaria canadensis***

In vitro studies showed that bloodroot extracts significantly influenced the proliferation of human PBMCs, with notable effects depending on plant organ and its interaction with extract type, although extract type alone was not significant. Most extracts enhanced PBMC proliferation. In contrast, studies on K562 cells revealed significant effects of organ, extract type, and their interaction. Notably, the rhizome alcohol extract markedly reduced K562 cell viability, eliminating visible cells, while flower and root alcohol extracts also showed a reduction trend, though leaf alcohol extract had no significant effect.(13) The findings demonstrated that sanguinarine inhibits proliferation of NPC cells in a time- and dose-dependent manner, affecting both low-differentiated CNE2 cells and highly metastatic 5-8F cells, along with reducing their colony-forming ability. Additionally, it suppresses the invasion and migration of these cancer cells.(14)

### **4. Network Pharmacology on *Sanguinaria canadensis***

This study identifies *Sanguinaria canadensis* as a promising natural inhibitor targeting CDK2 and AURKA. Through network pharmacology, bioinformatics, and computational analyses, *Sanguinaria canadensis* was found to regulate these key targets, leading to inhibition of DNA replication, disruption of DNA repair mechanisms, induction of apoptosis, and cell cycle arrest, thereby suppressing cancer growth. These findings suggest that combining *sanguinaria canadensis* with radiotherapy may offer significant therapeutic benefits, particularly for patients with advanced or treatment-resistant cancers.(15)

## 5. *Sanguinaria Canadensis* in Homoeopathic Pharmacopoeia of India (HPI)

As described in the Homoeopathic Pharmacopoeia of India, the crude drug of *Sanguinaria canadensis* consists of whole or fragmented rhizomes and roots. Macroscopically, the rhizome is horizontal, cylindrical, and slightly compressed, with a brown external surface and distinct scars, while fracture is short and uneven. Microscopical examination reveals an outer epidermal layer followed by a cortex composed of parenchymatous cells containing numerous starch grains and occasional oil globules. A well-defined vascular region with collateral bundles is present, separated by medullary rays. Characteristic latex-containing cells, often arranged in chains and filled with reddish contents, are distributed throughout the cortical and medullary regions.(16)

### Discussion

The medicinal potential of *Sanguinaria canadensis* (bloodroot) is primarily driven by its rich profile of bioactive isoquinoline alkaloids, most notably **sanguinarine** and **chelerythrine**, which exhibit significant antimicrobial, anti-inflammatory, and anti-proliferative properties. Research indicates that these compounds exert their effects through complex molecular mechanisms, such as inducing apoptosis, suppressing inflammatory mediators like TNF- $\alpha$  and IL-6, and modulating key signaling pathways including NF- $\kappa$ B and MAPK. While studies have highlighted the plant's ability to inhibit tumor growth, invasion, and angiogenesis—even showing synergy with antibiotics like kanamycin—its clinical transition remains heavily restricted by safety concerns, including potential cytotoxicity and reports of precancerous changes in oral tissues. Despite these challenges, *S. canadensis* maintains therapeutic relevance in systems like Homoeopathy, as documented in the Homoeopathic Pharmacopoeia of India (HPI), though bridging the gap between experimental pharmacology and standardized clinical application remains a critical priority for future research.

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