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Purpurin as a promising anticancer agent: A review of preclinical evidence

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ABSTRACT

Purpurin, a naturally occurring anthraquinone pigment, has gained attention for its promising anticancer properties. This systematic-narrative hybrid review summarises current preclinical evidence on its mechanisms of action, pharmacology, and translational potential. Literature searches were conducted using PubMed, Web of Science, Scopus, and Google Scholar up to June 2025. Purpurin demonstrates selective cytotoxicity across multiple cancer models through redox imbalance, mitochondrial dysfunction, inhibition of PI3K/AKT signalling, and upregulation of the tumour suppressor LHPP. It also interferes with amino acid and glutamine metabolism and suppresses oncogenic protein aggregation. As a photosensitiser, purpurin enhances photodynamic therapy through light-activated ROS generation. Despite these promising mechanistic insights, its clinical applicability remains limited by poor aqueous solubility, rapid metabolism, and insufficient pharmacokinetic and toxicological data. Early *in vivo* studies indicate favourable safety, and emerging nanoparticle-based delivery systems show potential to improve bioavailability and tumour targeting. Collectively, current findings highlight purpurin as a compelling candidate for further development in oncology, particularly as part of combination or photo-enhanced therapeutic approaches. Continued research is required to address existing pharmacological gaps and to evaluate purpurin in clinically relevant models.

1. Introduction

Anthraquinones (AQs) are a class of naturally occurring aromatic compounds widely distributed in various plant parts, including roots, rhizomes, fruits, and flowers [1]. Among these, the 9,10-anthraquinone isomer is particularly prominent and has long been used in dye production, paper bleaching, and as a pigment in food, pharmaceuticals, and cosmetics [2]. In addition to their industrial applications, many AQ derivatives exhibit diverse biological activities, including anticancer [3], antimicrobial [4], anti-inflammatory [5], and antioxidant [6] effects. AQ-based compounds, including mitoxantrone, pixantrone, and emodin, have demonstrated diverse therapeutic potential. These compounds are commonly used as chemotherapeutic agents [7,8] and laxatives [9], and are also being investigated for their efficacy in treating multiple sclerosis [10,11] and malaria [12,13].

A notable AQ derivative drawing increasing scientific interest is purpurin (1,2,4-trihydroxy-9,10-anthraquinone) as shown in Fig. 1. It is predominantly isolated from the roots of *Rubia* species, such as *Rubia tinctorum* (madder), *R. akane*, *R. cordifolia*, and *R. radix* [14]. Purpurin has historically been used as a dye [2,14], food colorant [15], and in traditional medicine [16]. Chemically, it has the molecular formula $C_{14}H_8O_5$, a molecular weight of 256.21 g/mol, and appears as orange crystalline needles [17]. While purpurin is known for its red pigment and diverse pharmacological activities, it is distinct from its derivative,

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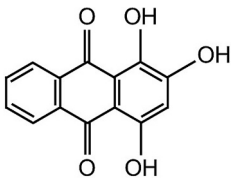

Fig. 1. Chemical structure of purpurin.

purpurin-18, which refers to a modified form of the molecule with specific structural substitutions. This review specifically focuses on the parent compound, purpurin, and its potential anticancer properties, distinguishing it from its derivatives like purpurin-18.

The growing interest in natural compounds for cancer treatment, especially anthraquinones like purpurin, highlights the shift toward exploring alternative therapeutic strategies in oncology. This trend is driven by the increasing demand for agents that not only target tumours selectively but also minimise the side effects typically associated with conventional chemotherapy. Its reported biological activities, which include antioxidant [18], antimutagenic [19], neuroprotective [20,21], antiadipogenic [22], and anticancer [23] effects, are largely attributed to its planar structure [24], which facilitates interactions with deoxyribonucleic acid (DNA) and regulatory proteins. In cancer models, purpurin was found to induce apoptosis [23], inhibit cell proliferation [23,25], and enhance photodynamic therapy (PDT) [26,27], making it a candidate of interest in cancer therapeutics. Also, purpurin attenuated tumour necrosis factor alpha/interferon-gamma (TNF-α/IFN-γ)-induced inflammation in a non-tumour human keratinocyte (HaCaT) cell line by inhibiting the activation of key signalling pathways such as protein kinase B (AKT), mitogen-activated protein kinases (MAPKs), and nuclear factor kappa B (NF-κB) [28].

Although several reviews have examined the biological activities of anthraquinones as a broad class [1,17,29–31], these works typically focus on widely studied compounds such as emodin and aloe-emodin and provide only limited coverage of purpurin. To date, no review has synthesised emerging preclinical evidence on purpurin's unique mechanisms, including its recently identified ability to modulate the tumour suppressor LHPP [32], its dual redox- and mitochondria-targeted cytotoxic actions, or its photodynamic and metabolic synergistic properties. Furthermore, nanoparticle-assisted delivery strategies [33–35] have not been comprehensively discussed in existing literature. This review therefore addresses a critical gap by consolidating and interpreting new mechanistic, pharmacological, and formulation-based insights that position purpurin as a distinct and promising anticancer candidate within the anthraquinone family.

2. Methodology

This work was conducted as a systematic-narrative hybrid review, combining systematic literature identification and screening with qualitative synthesis and interpretive discussion. The review methodology followed the principles of the PRISMA 2020 guidelines to the extent applicable to non-interventional preclinical literature reviews.

A systematic literature search was conducted using databases such as PubMed, Scopus, Web of Science, and Google Scholar from December 2024 to June 2025. The search terms comprised combinations such as "purpurin AND anticancer," "purpurin AND human cancer," "purpurin AND lung cancer," along with other cancer-related types including "colon cancer," "breast cancer," "cervical cancer," "prostate cancer," "adenocarcinoma," "melanoma," "carcinogenesis," and "tumour model," all connected with the Boolean operator "AND" alongside purpurin. In addition, related pharmacology terms including "cytotoxicity", "pharmacokinetics", and "preclinical studies" were also used for the purpurin literature search. Inclusion criteria were limited to original research articles published in English, focusing on preclinical *in vitro* or *in vivo* studies examining purpurin's anticancer mechanisms. Studies lacking relevance to the topic or published in languages other than English were excluded. The selected articles were analysed to extract data on purpurin's anticancer mechanisms, efficacy, delivery systems, and safety profiles. After applying the search terms and inclusion/exclusion criteria across the databases, a total of 4420 articles were initially found, of which 29 articles were included in this review and 4391 articles were excluded based on the inclusion and exclusion criteria.

A structured approach was applied to ensure transparency and reproducibility of the literature screening process. Following the initial database queries, all identified records were imported into a reference management system and screened in two stages: (1) title and abstract screening, and (2) full-text assessment. Two reviewers independently screened all records, with discrepancies resolved through discussion or by a third reviewer when needed.

Inclusion criteria were defined as:

(i) original research articles;
(ii) published in English;
(iii) presenting *in vitro*, *in vivo*, or mechanistic studies evaluating purpurin or purpurin-containing formulations in cancer or carcinogenesis-related models;
(iv) studies reporting specific anticancer, mechanistic, pharmacokinetic, toxicological, or delivery-related outcomes relevant to purpurin's biological activity.

Exclusion criteria included:

(i) non-English publications;
(ii) review articles, editorials, conference abstracts, or patents;
(iii) studies focusing solely on purpurin derivatives without assessing the parent compound;
(iv) reports lacking primary experimental data;
(v) studies examining purpurin for non-biological applications (*e.g.*, dyes, materials science) without relevance to cancer biology.

During full-text screening, articles were further excluded if they did not report adequate methodological detail, lacked extractable outcome data, or did not directly investigate purpurin's biological effects. Of the 4420 records initially retrieved, 3857 were removed during title and abstract screening due to irrelevance or duplication. The remaining 563 articles underwent full-text review, where 534 were excluded based on the criteria above. Ultimately, 29 studies met all inclusion criteria and were incorporated into this review.

To ensure consistent data extraction, all included studies were reviewed using a structured template capturing: experimental model (cell line or animal type), purpurin formulation, dosage, exposure duration, mechanistic endpoints, and major findings. This process ensured a standardised comparison across heterogeneous study designs and minimised bias in the synthesis of evidence. A PRISMA flow diagram summarising the study selection process is portrayed in Fig. 2.

3. Anticancer potential of Purpurin

Purpurin's anticancer potential is attributed to its multifactorial mechanisms of action, which make it a highly promising candidate for cancer treatment. These mechanisms not only target specific cancer hallmarks but also offer new avenues for drug development. This section elaborates on purpurin's multifaceted approach to cancer therapy.

3.1. Antimutagenic properties

Purpurin has demonstrated protective effects against alcohol-induced hepatotoxicity primarily through its reactive oxygen species (ROS)-scavenging activity and the upregulation of nuclear factor