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Aloe-Emodin and Emodin's Role in Premalignant Lesions of the Oral Cavity Cancers and Other Organs

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Abstract

Oral squamous cell carcinoma (OSCC) is one of the commonest cancers globally. Prevalence of the disease is high in the third world countries of South-east Asia, specifically tied to inherent abuse of tobacco and areca nuts. The disease manifests as oral potentially malignant disorders, such as OED, OSMF, leukoplakias, etc., that provides avenues for effective control early in the sequence of cancer progression and immune evasion. Focus of our study was to gather insights on the potential of natural, biological molecules to intervene early in the carcinogenesis processes.

We present herewith, a review of literature and plausible mechanism of action studies carried out widely in cellular or animal models, that remains to be translated successfully to the clinics. We also, discuss further, how green bio-manufacturing methodologies may hasten the process of bringing these molecules for mitigating oral public health challenges, effectively; in a multidisciplinary approach. Further, human studies in blinded clinical trials, is however warranted to ascertain clinical efficacy and safety. In summary, aloe-emodin stands out among anthraquinones for its enhanced anticancer potency and broader therapeutic applications, making it a valuable compound in both research and clinical settings.

Keywords: Antibacterial; Anti-Inflammatory; Aloe-Emodin; Emodin; OSCC; Toxicity; Efficacy; Cancer, Immune System

Abbreviations

CAFs: Cancer associated fibroblasts, CSCs: Cancer Stem Cells, JAK: Janus Kinases, AKT: Ser/Thr Protein KinaseB, STAT3: Signaling and transduction activated transcription factor 3, MMP: Matrix-MetalloProteinases, EGF; Epidermal growth factor, FAK: Focal adhesion Kinase, FGF: Fibroblast Growth Factor, (IL-1b, IL-6, IL-8): Interleukins 1beta, 6 and 8, TNFa: Tumor Necrosis factor-alpha, TGFb: Tumor Growth Factor-beta, PDGF, Platelet derived Growth Factor, MFI2: Melanotransferrin, MIF; Macrophage migration inhibitory factor M1/M2: Tumor-associated Macrophage (TAM) polarization states, N1/N2: Tumor-associated Neutrophil (TAN) polarized states, P.gingivalis, F.nucleatum: Oral bacteria Porphyromonas gingivalis and Fusobacterium nucleatum

Introduction

Oral squamous cell carcinoma (OSCC) is one of the most common cancers globally, with increased incidence rates in South and East- Asian countries. The global incidence exceeds 389000 cases annually as per a recent report quoting GLOBOCAN and is predicted to increase more than 65% each year [1]. These are a group of malignant tumors that develop in the mouth, throat, and upper respiratory tract squamous cells. Oral Epithelial Dysplasia (OED) is a term used to describe abnormal premalignant changes in the cells of the mouth. Dysplasia can be a precursor to cancer but does not always progress to malignancy. Oral submucous fibrosis (OSMF) and leukoplakias, are other premalignant conditions currently relegated to wait and watch health policy or surgical resections, without giving heed to 'field cancerization' problems associated with mucosal cancers.

Aloe-emodin and emodin, are anthraquinone compounds found in various plants that have shown promising anticancer properties, particularly in Oral Cancers. The structural and physicochemical nuances of the molecules can be visualised and analyzed (Figure 1). Research indicates that both aloe-emodin and emodin can inhibit the growth of oral squamous cell carcinoma

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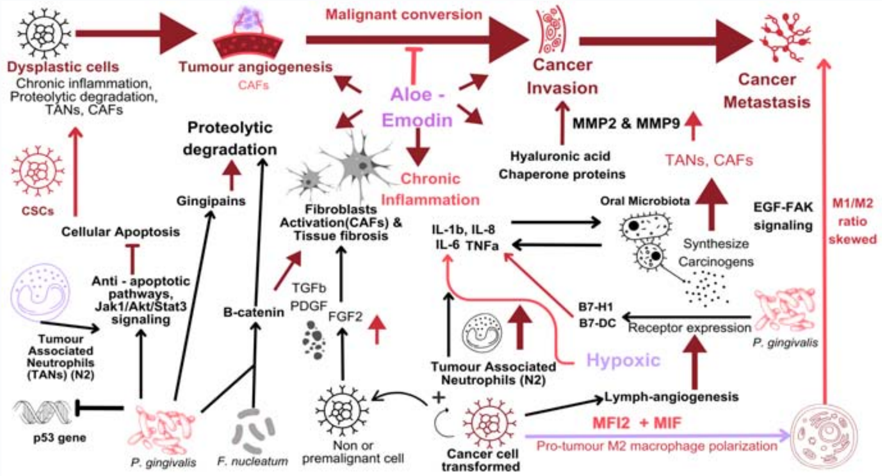

Graphical Abstract: The simmering Oral Tumor Micro-Environment has potential to benefit from aloe-emodin therapy. The figure was drawn on CanvaTM design software.

(OSCC) by inducing apoptosis and affecting critical cellular pathways [Stompor-Gorący M 2021].

To elaborate on structural differences between the two molecules, the methyl group in emodin plays a significant role in enhancing its biological functions and therapeutic properties. The methyl group also contributes to the stabilization of the molecule, which is essential for its interaction with reactive oxygen species (ROS). This methyl group is missing in Aloe-emodin.

Objectives

We aimed to investigate recent advances in development of oral cancer therapies based on aloe-emodin and emodin molecules in this review article and included major reports from the last two decades on the topic, to have an all-round view of its therapeutic potential.

Method and Results

Medical literature databases, such as Pubmed, Google scholar, Medline, were queried using keywords mentioned above, and resultant full-text articles in English, and relevant keywords containing [xx] articles were reviewed; after removal of duplicates and articles in vernacular languages.

Discussions

Aloe-emodin and emodin, both the anthraquinones have a complex triple organic ring structures that includes a methyl group at position 6 of its anthraquinone ring in emodin, but absent in aloe-emodin; as delineated before in introduction section, and therefore contributes to its diverse, albeit distinct pharmacological effects [18, 52]. Aloe-emodin, a naturally occurring anthraquinone, is found primarily in the aloe plants, particularly in *Aloe vera,* an ubiquitous succulent.

Pharmacological properties of Aloe-emodin

***Laxative Effects*:** Aloe emodin is well-known for its stimulating, laxative properties, which are attributed to its ability to activate CFTR chloride channels in the colon, enhancing fluid secretion and enhanced aquaporin3 expression [59, 79].

***Anticancer Activity*:** Research indicates that aloe-emodin exhibits anticancer effects by inducing apoptosis in various cancer cell lines, including cervical, pancreatic, prostate, and glioma cells. It disrupts mitochondrial membrane potential and activates both apoptotic and autophagic pathways [24, 38, 39, 62, 76].

***Other Biological Activities*:** The compound also shows antiviral, anti-inflammatory, antibacterial, antiparasitic, neuroprotective, and hepatoprotective activities. These properties suggest its potential use in treating diseases such as Alzheimer's, liver fibrosis, and various cancers.

***Toxicity Concerns*:** Despite its beneficial effects, aloe-emodin has been associated with hepatotoxicity and nephrotoxicity. Its pharmacokinetics indicate poor intestinal absorption and low bioavailability, raising concerns about its safety profile.

To summarize the effects, aloe-emodin is a compound of significant interest for its diverse pharmacological activities, particularly in cancer therapy, alongside notable safety considerations. Aloe emodin exhibits superior effectiveness compared to other anthraquinones, particularly in anticancer applications. Here are key comparisons based on recent studies:

***Anticancer Efficacy*:** Aloe emodin has been shown to reduce cell viability more effectively than emodin in cancer cell lines such as melanoma (MUG-Mel2) and oral squamous cell carcinoma (SCC-25). In a study, aloe-emodin at 20 μM concentration resulted in greater cell death than emodin in these cancer types, indicating its superior cytotoxic effects against certain tumors [52].

Aloe-emodin also demonstrates a broad spectrum of other pharmacological activities, including anti-inflammatory, antibacterial, and antiviral effects [22]. These properties make it a versatile candidate for therapeutic applications beyond cancer treatment, such as in psoriasis management, where it outperformed tacrolimus cream in reducing epidermal thickness and inflammation [55].

***Pharmacokinetic Interactions*:** Aloe-emodin can influence the pharmacokinetics of other anthraquinones. It tends to increase the plasma exposure of compounds like rhein and physcion while decreasing that of emodin when co-administered together. This suggests that aloe-emodin may enhance the overall therapeutic profile of anthraquinone combinations [1, 42].

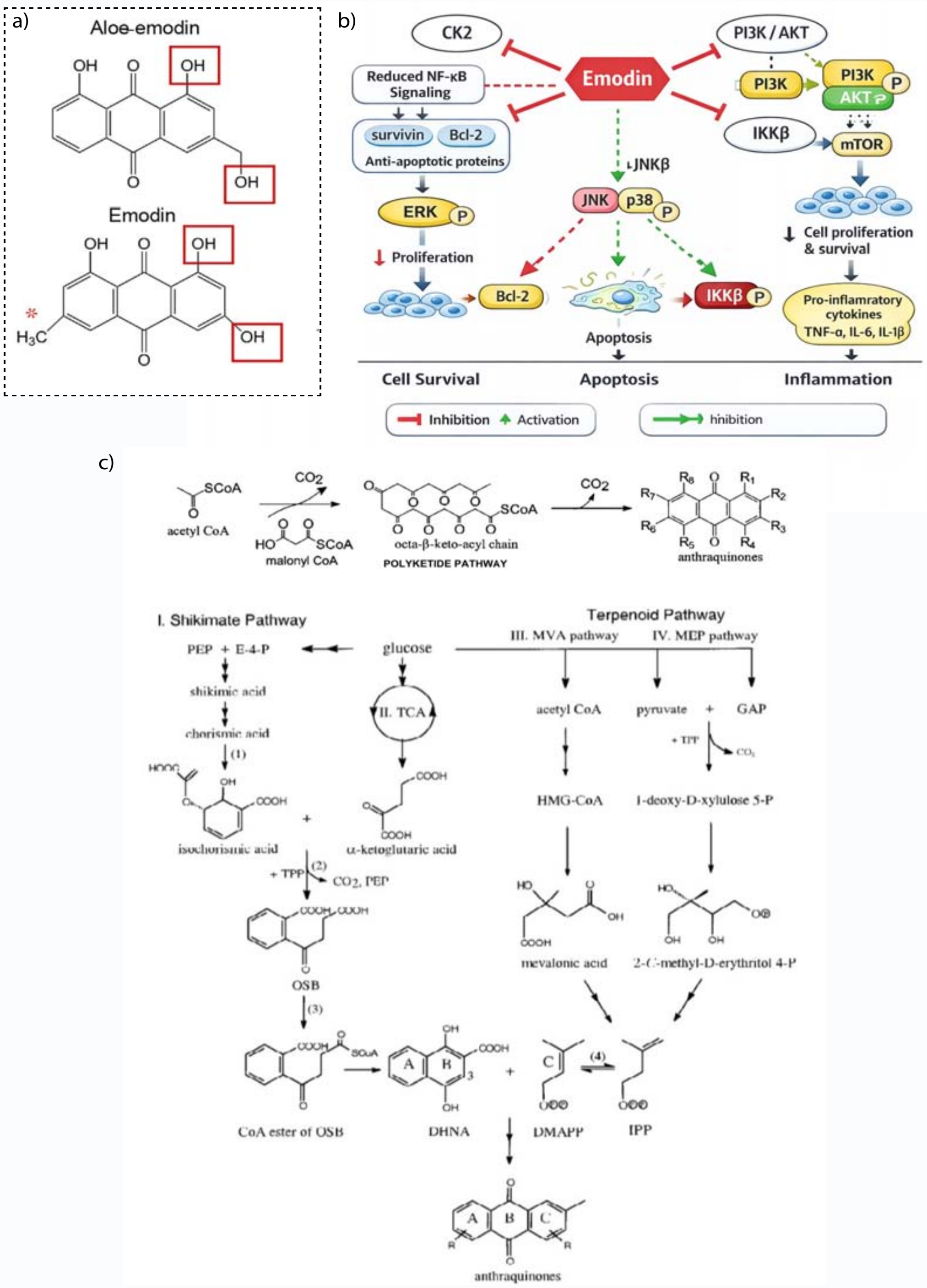

Figure 1: Chemical Structure of **Aloe-emodin and emodin** secondary metabolites **(***box* **a)** with extra methyl functional group* for emodin, and its biochemical synthesis pathways **(b)** in nature, other than mammals (PubChem CID:3220 ; CHEBI:42223; Han YS 2001).
a. Chemical Structure, and **b.** Mechanistic relevance of Emodin molecule against tumors progressive towards malignant transformation, **c.** Polyketide pathway and Shikimate-Mevalonate pathways (in higher plants) of anthraquinone biosynthesis.

***Comparative Effectiveness*:** In terms of specific therapeutic outcomes, aloe-emodin has been reported to have stronger anti-psoriatic effects compared to other anthraquinones, highlighting its potential as a safer alternative for long-term treatment [10, 55].

Structural connotations, Biological Activities and Mechanisms of Emodin

***Antioxidant Activity*:** The presence of the methyl group is believed to influence the compound's ability to scavenge free radicals, thereby enhancing its antioxidant properties. This is crucial for protecting cells from oxidative stress, which is linked to various diseases, including cardiovascular disorders [25].

***Anti-inflammatory Effects*:** Emodin exhibits anti-inflammatory properties that are partially attributed to the methyl group. It modulates various signaling pathways involved in inflammation, such as inhibiting the expression of pro-inflammatory cytokines and enzymes, thus enabling the recognition of cancerous cells in tumor milieu [Stompor-Gorący M. 2021].

Cardiovascular Protection**:** The methyl group enhances emodin's cardioprotective effects by improving its interaction with cellular targets in the heart. It aids in the regulation of calcium channels and myocyte contraction, contributing to vasodilation and reduced hypertension [25].

Anticancer Properties**:** Emodin's methyl group also plays a role in its anticancer effects by modulating cell signaling pathways associated with tumor growth and metastasis. Specifically, the methylation can affect gene expression and protein interactions that are critical in cancer biology [Stompor-Gorący M. 2021].

Metabolic Regulation**:** The methyl group contributes to emodin's ability to regulate glucose metabolism and lipid profiles, making it beneficial for conditions such as diabetes and metabolic syndrome [25]. In summary, the methyl group in emodin significantly enhances its biological activities by influencing its chemical interactions and mechanisms of action across various therapeutic areas.

Poly-pharmacological mechanisms of action of the natural compounds

Induction of Apoptosis**:** Emodin has been demonstrated to trigger apoptosis in OSCC cells, such as SCC-4 and SCC-15 lines. This involves the activation of caspases and modulation of Bcl-2 family proteins, leading to programmed cell death [9, 41].

Inhibition of Migration and Invasion**:** Emodin reduces the migration and invasion capabilities of cancer cells by downregulating matrix metalloproteinases (MMPs), particularly MMP-2 and MMP-9, which are crucial for tumor metastasis [9, 39].

Cell Cycle Arrest**:** The compound also causes cell cycle arrest at various phases, preventing cancer cell proliferation. This was observed in studies where emodin-treated cells showed significant reductions in cell division rates [1, 39].

Additional Benefits**:** Emodin's broad-spectrum anticancer effects extend beyond oral cancer [76-81]; as has been noted for its ability to combat multidrug resistance in cancer cells and exert immunomodulatory effects. Its mechanisms include anti-inflammatory and antiangiogenic actions, making it a potential candidate for combination therapies in cancer treatment [1, 39].

Effectiveness of Emodin in comparison to other cancer treatments

Emodin exhibits notable anticancer properties, particularly when compared to conventional treatments and other natural compounds. Here's a comparison of emodin's effectiveness in treating cancer:

a. Emodin vs. Conventional Cancer Treatments

Synergistic Effects**:** Emodin has been shown to enhance the efficacy of standard chemotherapy drugs such as gemcitabine, cisplatin, and paclitaxel. Studies indicate that when combined with these agents, emodin can significantly increase apoptosis rates in resistant cancer cell lines, suggesting it may help overcome drug resistance [1].

Targeted Action**:** Unlike some conventional treatments that can affect both cancerous and healthy cells, emodin has been noted for its ability to selectively target cancer cells while sparing normal cells. This selective action minimizes side effects, a common drawback of traditional chemotherapy [52].

b. Emodin vs. Other Natural Compounds

Comparison with Aloe-Emodin: In studies comparing emodin with aloe-emodin, the latter exhibited stronger effects on reducing cell viability in certain cancer cell lines. For instance, aloe-emodin showed greater potency than emodin in melanoma and squamous cell carcinoma cells [52]. However, emodin still holds significant promise due to its broader range of anticancer mechanisms.

Mechanisms of Action: Emodin operates through various pathways, including apoptosis induction and inhibition of tumor migration and invasion. It affects signaling pathways like TGF-β and Wnt/β-catenin, which are crucial in cancer progression [37].

Emodin's efficacy compared to traditional chemotherapy agents

Emodin demonstrates significant potential as an adjunct to traditional chemotherapy agents, enhancing their efficacy while potentially reducing side effects. Here's how emodin compares to conventional treatments:

Efficacy Comparison:

Synergistic Effects**:** Emodin has been shown to enhance the effectiveness of various chemotherapeutic agents, including gemcitabine, cisplatin, and paclitaxel. Studies indicate that when used in combination with these drugs, emodin can increase apoptosis rates and improve overall tumor suppression compared to chemotherapy alone [1, 29, 71].

Emodin is known to operate through multiple mechanisms, including the induction of reactive oxygen species (ROS), modulation of apoptosis-related proteins (like Bcl-2 and Bax), and inhibition of pathways such as NF-κB. These actions contribute to its ability to sensitize cancer cells to chemotherapy, making them more susceptible to treatment [1, 58, 71].

Reduced Toxicity**:** The combination of emodin with traditional chemotherapy may allow for lower doses of the chemotherapeutic agents, thereby reducing their toxicity. For instance, emodin has been reported to enhance the antitumor effects of gemcitabine even at lower doses, minimizing adverse effects associated with higher doses of chemotherapy [1].

Clinical Implications:

Tumor Growth Inhibition**:** In preclinical studies, emodin has effectively suppressed tumor growth in various cancer models when combined with standard chemotherapy. This suggests that it could be a valuable addition to treatment regimens for cancers such as pancreatic, prostate and colorectal cancer [1, 24, 29, 71].

Potential for Overcoming Resistance**:** Emodin has shown promise in overcoming drug resistance in cancer cells, which is a significant challenge in chemotherapy. By downregulating proteins associated with resistance mechanisms, emodin may enhance the effectiveness of existing treatments [1, 71].

Potential benefits of using emodin over traditional chemotherapy

Emodin offers several potential benefits over traditional chemotherapy agents, making it an attractive option for cancer treatment. Here are some key advantages:

Table 1: Aloe-emodin and emodin specific studies testing efficacy in Oral Cancer.

Natural compound	Effect in Oral Cancer	Mechanism of Action (MoA)	Refs.
Aloe-emodin	Inhibits oral cancer (KB) cell growth; induces cell cycle arrest in G2/M phase; increases ALP activity; no DNA fragmentation observed	Cell cycle arrest at G2/M; anti-proliferative; modulates mitochondrial function and redox state; increases caspase activity and ROS; reduces DNA repair enzyme expression (DNA-PK, BRCA1, ATM); decreases MMP-2 and NF-κB (reducing migration/ invasion)	[58]
Aloe-emodin	Inhibits viability and migration of tongue squamous cell carcinoma (SCC-4); induces S phase arrest and apoptosis	Increases ROS, intracellular calcium, caspases-3/8/9; decreases mitochondrial membrane potential; downregulates DNA repair enzymes; inhibits MMP-2 and NF-κB	[57]
Emodin	Reduces viability of tongue squamous cell carcinoma (SCC-4); strongest cytotoxic effect among related anthraquinones	Induces DNA damage; inhibits DNA repair enzymes (DNA-PK, BRCA1, ATM); inhibits MMP-2 and NF-κB; induces cell cycle arrest and apoptosis	[57]
Emodin	Inhibits proliferation of tongue squamous cell carcinoma (SCC25) in vitro	Induces cytotoxicity in cancer cells; comparable or synergistic with 5-fluorouracil	[58]
Aloe-emodin & Emodin	Both reduce migration/invasion and viability of oral cancer cells (SCC-4, SCC25)	Downregulate MMP-2, NF-κB; inhibit DNA repair; induce apoptosis via caspase activation and ROS generation	[57, 58]

Enhanced efficacy due to *synergistic effects*: Emodin has been shown to enhance the effectiveness of conventional chemotherapy drugs like gemcitabine and cisplatin. For instance, studies indicate that combining emodin with gemcitabine can significantly increase tumor suppression and apoptosis rates compared to using gemcitabine alone, even at lower doses [71].

Overcoming Drug Resistance: Emodin can reverse resistance to chemotherapy in certain cancer types. It has demonstrated the ability to sensitize resistant cancer cells, such as those in chronic myeloid leukemia, to standard treatments like imatinib [Stompor-Gorący, M 2021].

Reduced Toxicity and Lower Side Effects: Traditional chemotherapy often comes with severe side effects due to its impact on healthy cells. Emodin's selective action on cancer cells may allow for reduced dosages of chemotherapeutic agents, thereby minimizing toxicity and improving patient quality of life [19, 71].

Poly-pharmacological mechanisms of action of emodin

Diverse Anticancer Mechanisms**:** Emodin operates through various pathways, including apoptosis induction, inhibition of angiogenesis, and modulation of inflammatory responses. Its ability to target multiple molecular pathways can enhance its overall effectiveness against tumors [71].

Regulation of Key Proteins**:** Emodin has been shown to downregulate proteins associated with survival and proliferation in cancer cells, such as survivin and Bcl-2. This regulation contributes to its pro-apoptotic effects and can improve the overall response to treatment [34, 71].

Anti-inflammatory and Antioxidant Properties of Emodin

Emodin is a bioactive compound known for its various therapeutic effects, particularly in the context of inflammation and cancer. One of its notable interactions is with the ***Macrophage Migration Inhibitory Factor (MIF),*** which plays a significant role in linking inflammation to cancer progression.

Emodin and MIF Interactions:

Role of MIF in cancer progression: MIF is involved in promoting inflammation and has been implicated in tumor growth by enhancing angiogenesis through the upregulation of Vascular Endothelial Growth Factor (VEGF) secretion [68, 80].

As stated earlier, emodin acts as a reactive oxygen species (ROS) generator and inhibits hypoxia-inducible factor 1 alpha (HIF-1a), which is crucial for MIF's role in cancer. By downregulating HIF-1a activity, emodin disrupts the pro-tumorigenic signaling pathways associated with MIF, leading to reduced tumor growth and angiogenesis [68, 80].

Effects on Cancer Cells: In studies involving prostate cancer cells, emodin has been shown to enhance ROS levels and inhibit pathways that would typically promote cancer cell survival and proliferation. This includes preventing the nuclear translocation of the androgen receptor (AR) and promoting its degradation, which is significant in hormone-sensitive cancers [Tu Y 2019; Wang SS 2017]. Studies also suggest that Melanotransferrin (MFI2 or CD228) plays a significant role in the malignant transformation of oral precancerous lesions by facilitating cell proliferation, migration, and invasion, key characteristics of cancer development [78].

Therapeutic Implications:

Emodin's ability to modulate MIF activity suggests potential therapeutic applications in treating cancers characterized by high inflammatory responses. Its effects on reducing MIF expression and inhibiting angiogenesis could be beneficial in managing tumor growth and metastasis [26].

Overall, emodin represents a promising candidate for further research into its anti-cancer properties, particularly through its interactions with inflammatory mediators like MIF.

Additional Health Benefits**:** Beyond its anticancer effects, emodin possesses strong anti-inflammatory and antioxidant properties.

These benefits can help mitigate inflammation associated with cancer and improve overall health outcomes during treatment [19, 44, 77].

Side effects of emodin in cancer patients

Like most anticancer medications, the most common side effects of emodin in cancer therapy are due to ***overdosages*** exceeding 500 mg/kg body weight *in vivo*; as determined in some animal model preclinical studies and are mentioned below:

Hepatotoxicity**:** Emodin can cause liver damage, leading to elevated liver enzymes and impaired liver function, especially with prolonged use or high doses [1, 19, 75].

Nephrotoxicity**:** Kidney toxicity is another reported side effect, potentially resulting in reduced kidney function [1, 19, 75].

Reproductive Toxicity**:** Emodin may impair sperm motility and embryonic development, posing risks for fertility and pregnancy [1, 19, 75].

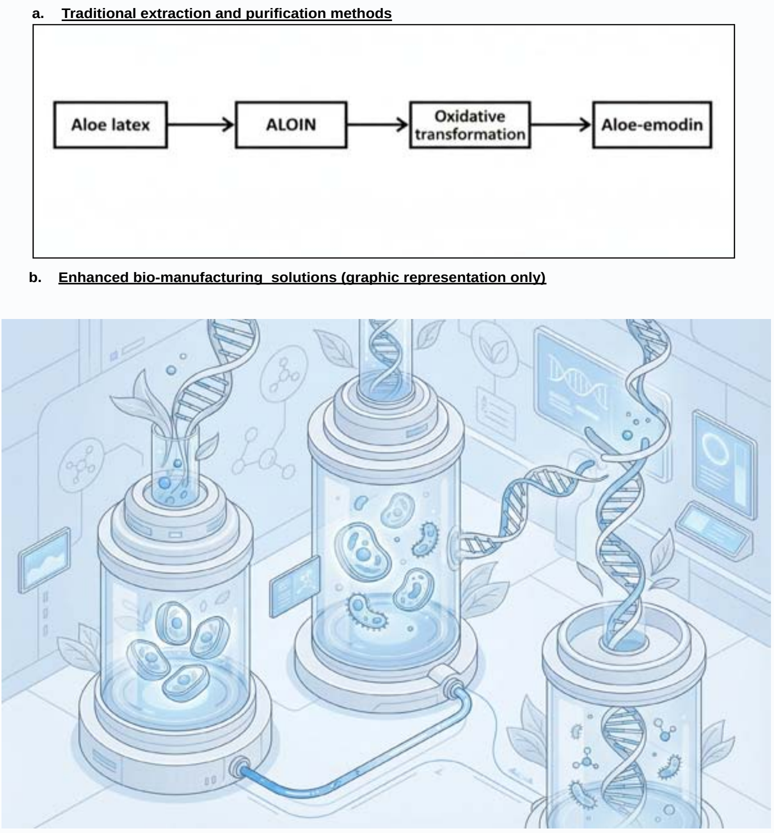

Figure 2: Potential bio-manufacturing paradigms for production of anthraquinones- aloe-emodin and emodin in lower eukaryotes or their natural plant cells in secondary tissue-culture and controlled bioprocessing.

***Gastrointestinal Issues*:** It can cause severe diarrhea, abdominal pain, and electrolyte imbalances due to its anthraquinone laxative properties [1, 19].

***DNA Damage and Mutagenicity*:** Emodin has been linked to DNA damage and mutagenic effects at certain concentrations, raising concerns about its long-term safety [1, 19, 39].

These side effects highlight the need for careful monitoring and dosage control during any emodin-based cancer therapy. The effective dosage (ED50) however shows bioactivity ranges between 10 to 40 mg/kg, ie. 10-fold less than toxic doses [32, 71, 77], thus leaving a wide window, nonetheless.

Extraction and purification protocols of aloe-emodin and emodin for bio-manufacturing

Aloe-emodin can be extracted from the aloe plant using several methods, primarily focusing on the oxidation of aloin, a compound found in aloe latex. Here are the main extraction processes, as depicted below.

Extraction methods:

The most common method involves ***oxidizing*** aloin using an oxygen-containing gas in an acidic medium. This process often employs catalysts like copper salts and can achieve high yields of aloe-emodin. For instance, aloin is treated with hydrochloric acid and oxygen, resulting in aloe-emodin after several hours of reaction time.

Solvent-based Extraction*:* Aloe emodin can also be extracted using organic solvents such as toluene or dichloromethane through techniques like Soxhlet extraction. This method allows for the separation of aloe emodin from the plant material effectively.

Crystallization*:* After extraction, crude aloe-emodin can be purified through crystallization, where it forms orange needle-like crystals upon cooling the solution.

These methods highlight the versatility in extracting aloe emodin from aloe plants, ensuring both efficiency and purity for further applications in pharmaceuticals and other fields.

Advanced bio-manufacturing paradigms

The synthesis of anthraquinones occurs via two main pathways, *polyketide* pathway and the *shikimate* pathway. The former operates in bacteria, fungi, and plants, whereas the latter is known to be exclusive to plants [36].

With the advent of recombinant DNA technology, lower eukaryotes or plant cells amenable to genetic or epigenetic modifications, can be metabolically engineered to mass produce a natural molecule, perfectly in sync with nature, and green processes. The potential of transferring this capability for advanced bio-manufacturing is illustrated in Figure 2.

Overall, our article reviews benefits of utilizing molecules from nature, without compromising on quality, efficacy and mitigating side-effects for developing affordable cancer therapies, taking oral cancer as an example.

Key Findings on Emodin's Interaction with EGFR and FAK, (*the receptor tyrosine kinases*) involved in OSCC

EGFR Inhibition*:* Emodin has been found to exhibit strong binding interactions with EGFR, which may enhance the sensitivity of cancer cells to EGFR inhibitors. This is particularly relevant in cancers where EGFR plays a critical role in tumor growth and resistance to therapies.

***Synergistic Effects*:** Studies indicate that emodin can sensitize pancreatic cancer cells to EGFR inhibitors, suggesting that it may enhance the effectiveness of existing treatments by overcoming resistance mechanisms associated with aberrant EGFR signaling [24, 65].

***FAK Inhibition*:** FAK is known to play a significant role in cancer cell survival and migration. Targeting FAK in combination with EGFR inhibition could lead to improved therapeutic outcomes. The combination of FAK inhibitors with EGFR TKIs (tyrosine kinase inhibitors) has been shown to reduce cell viability more effectively than either treatment alone, especially in resistant non-small cell lung squamous carcinoma (NSCLC) cell lines.

Emodin's anticancer effects may involve the modulation of various signaling pathways, including those related to MEK2, ERK1, and p38 MAPK, which are crucial for cell proliferation and survival. By influencing these pathways, emodin may enhance the efficacy of therapies targeting both EGFR and FAK, that promotes invasion and metastasis in OSCC.

In summary, emodin's ability to interact with both EGFR and FAK presents a promising avenue for enhancing cancer treatment strategies, particularly in cases where resistance to standard therapies is observed. Further research is needed to fully understand its mechanisms and optimize its use in clinical settings.

Conclusions

Overall, Aloe-emodin and emodin both represent a promising therapeutic agent against oral cancer due to its multifaceted mechanisms that include apoptosis induction, migration inhibition, and cell cycle regulation. Aloe-emodin presents a compelling option as a complementary therapy alongside traditional treatment regimens due to its ability to enhance efficacy and reduce resistance. While it may not yet replace standard therapies, its unique properties and mechanisms position it as a valuable candidate for further clinical exploration in cancer treatment strategies. More clinical trials are needed to fully establish the efficacy and safety of aloe-emodin in cancer treatment, and its ability to enhance traditional chemotherapy agents; further positions it as a promising complementary therapy. Aloe-emodin and emodin's poly-pharmacological mechanisms of action and potential to reduce chemotherapy-related toxicity, while enhancing chemo-sensitivity and overcoming chemoresistance, makes it an interesting candidate for further exploration in solid tumor oncology as supported by various studies and reports.

Aloe-emodin, also presents a promising alternative or adjunct to traditional chemotherapy by enhancing efficacy, reducing toxicity, and employing multiple mechanisms of action against cancer. More basic, translational and clinical research on bioavailable, nano-delivery versions, such as improved gel and mouthwash formulations are needed to fully establish its role in preventive oncology; as also its potential benefits make it a compelling candidate for development of future cancer therapies. In summary, aloe-emodin stands out among anthraquinones for its enhanced anticancer potency and broader therapeutic applications, making it a valuable compound in both research and clinical settings.

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