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Review Article

AI-Driven Marine Bioactives for Cancer Therapy: A Systematic Review of Drug Discovery, Resistance Overcoming Strategies, and Precision Drug Delivery

Abdullah Faisal Albukhari*

Department of Medicine, Faculty of Medicine, King Abdulaziz University, Rabigh, SAUDI ARABIA.

ABSTRACT

Cancer continues to pose a significant global health challenge, with existing treatment options encountering obstacles such as drug resistance, systemic toxicity, and limited bioavailability. Marine ecosystems present a largely underutilized source of bioactive compounds that possess strong anticancer properties. The advent of Artificial Intelligence (AI) is transforming the landscape of drug discovery by improving the identification, optimization, and delivery processes for these marine-derived bioactives. This systematic review seeks to: (1) examine marine-derived anticancer bioactives along with their mechanisms of action and clinical significance; (2) evaluate AI-driven approaches in the discovery and screening of marine compounds; (3) investigate AI-based strategies for addressing drug resistance; and (4) assess AI-guided precision delivery methods for marine-derived anticancer agents. A thorough literature search was performed utilizing databases such as PubMed, Web of Science, Scopus, and Google Scholar. Studies were selected based on their investigation into marine bioactives with anticancer effects, AI-assisted drug discovery techniques, AI-enhanced mechanisms related to drug resistance, or AI-supported delivery systems. Data extraction centered on the sources of bioactives, molecular mechanisms involved, types of AI models applied, and stages of clinical translation. Notable marine-derived compounds like Trabectedin, Salinosporamide A, and Fucoidan demonstrate significant anticancer effects through mechanisms including apoptosis induction, angiogenesis inhibition, and targeting proteasomes. Computational models utilizing AI enhance the screening process for marine bioactives via high-throughput virtual screening methodologies, molecular docking analyses, and Quantitative Structure-Activity Relationship (QSAR) modeling. Analysis of drug resistance driven by AI identifies relevant biomarkers, refines therapeutic regimens, and forecasts tumor responses. Moreover, nanoparticle-based delivery systems optimized by AIalongside liposomes and hydrogel formulations-enhance drug stability, improve bioavailability levels, and increase efficiency in targeting tumors. AI is reshaping the field of cancer drug discovery from marine sources by expediting compound identification processes while optimizing treatment strategies and customizing drug delivery methods. Future investigations should prioritize expanding databases focused on AI-powered marine bioactives; refining predictive models applicable in clinical settings; and developing sustainable bioprospecting strategies driven by AI. Approaches guided by AI hold considerable promise in overcoming challenges associated with drug resistance while enhancing both precision and effectiveness in therapies derived from marine sources. A systematic review was conducted to assess the effects of AI-enhanced marine bioactives on cancer treatment. The study selection process is depicted in Figure 1 (PRISMA Flow Diagram). Initially, a total of 3,200 records were identified through searches in several databases, such as PubMed, Web of Science, Scopus, and Google Scholar. Additionally, 100 records were sourced from other avenues. After removing 600 duplicate entries, 2,700 studies remained for further screening. The titles and abstracts of these 2,700 records were carefully examined, leading to the exclusion of 2,000 records that did not meet the inclusion criteria. This included studies on irrelevant topics, those unrelated to cancer treatment, non-marine bioactives, or articles lacking AI methodologies. From the remaining articles, 700 full-text publications were assessed for eligibility. Following an in-depth evaluation process, 400 full-text articles were excluded due to various reasons such as inadequate AI integration, lack of relevance to marine bioactives, or being review articles instead of original research. In the end, a total of 300 studies were included in the qualitative synthesis (systematic review), while an additional 150 studies qualified for quantitative synthesis (meta-analysis where applicable). This PRISMA flow diagram (Figure 1) offers a clear and transparent depiction of the study selection methodology utilized in this research project, ensuring both reproducibility and methodological rigor.

Keywords: Artificial Intelligence, Marine Bioactives, Cancer Therapy, Drug Resistance, Precision Medicine, Drug Delivery.

Correspondence:
Mr. Abdullah Faisal Albukhari
Department of Medicine, Faculty of Medicine, King Abdulaziz University, Rabigh-21911, SAUDI ARABIA.
Email: aabdulqaderalbukhari@stu.kau.edu.sa

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INTRODUCTION

Cancer continues to be a significant contributor to illness and death globally, with approximately 19.3 million new diagnoses and 10 million deaths attributed to cancer recorded in 2020.[1-3]

Despite notable progress in chemotherapy, radiotherapy, and immunotherapy, existing cancer treatment methods encounter substantial challenges. These include issues such as drug resistance, systemic toxicity, and inadequate bioavailability, which contribute to less than ideal therapeutic results.[4] Drug resistance continues to pose a significant challenge, as numerous tumors acquire adaptive strategies that diminish the effectiveness of treatments. This situation underscores the ongoing need to discover new anticancer agents.[5]

Marine ecosystems represent a significant, underexplored source of bioactive substances that exhibit potential anticancer effects.

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Covering more than 70% of the planet's surface, oceans are home to a wide variety of marine life that generates distinctive secondary metabolites with strong biological activity.[6] Numerous compounds obtained from marine sources have shown significant potential in cancer treatment, with a few already being utilized in clinical settings. One such compound, Trabectedin, which is extracted from the tunicate species *Ecteinascidia turbinata*, has received approval for use against soft tissue sarcoma and ovarian cancer because of its capacity to disrupt DNA transcription and promote programmed cell death.[7] Salinosporamide A, a secondary metabolite derived from the marine bacterium Salinispora tropica, has demonstrated significant inhibitory effects on the proteasome and exhibits activity against multiple myeloma.[5-8] Likewise, Fucoidan, a sulfated polysaccharide sourced from brown algae, has shown properties that inhibit angiogenesis, modulate immune responses, and induce apoptosis in several types of cancers, such as liver and colorectal cancer (Figure 2).[9]

Artificial Intelligence (AI) has become a pivotal resource in expediting the process of drug discovery, improving drug delivery systems, and forecasting mechanisms of drug resistance. Models powered by AI have markedly improved the detection of bioactive compounds derived from marine sources by utilizing techniques such as high-throughput screening, molecular docking, and Quantitative Structure-Activity Relationship (QSAR) modeling.[10-14] AI-driven platforms have advanced drug formulation approaches by refining nanoparticle delivery systems, which in turn boost the stability, solubility, and tumor-targeting effectiveness of anticancer agents sourced from marine environments.[15] Additionally, bioinformatics tools powered by AI can forecast patterns of drug resistance through the analysis of genomic data from tumors, facilitating the creation of precision oncology approaches aimed at addressing therapeutic resistance.[13,15,16]

Despite the encouraging possibilities presented by marine bioactive compounds and the use of AI in cancer therapy, this area is still relatively uncharted. Existing studies mainly concentrate on synthetic and land-based compounds, with a scarcity of comprehensive evaluations regarding AI-facilitated marine drug discovery and its role in addressing drug resistance while improving targeted drug delivery.[10,14,15] This review seeks to address the existing knowledge gap by methodically examining the contributions of AI in the identification, enhancement, and clinical application of anticancer agents derived from marine sources.

OBJECTIVES

This systematic review aims to achieve the following objectives:

Comprehensive Analysis of Marine-Derived Anticancer Bioactives:

To conduct a thorough review and assessment of existing bioactive compounds derived from marine sources that exhibit anticancer characteristics, focusing on their origins, modes of action, and significance in clinical applications.[17,18]

Evaluation of AI's Role in Drug Discovery and Precision Medicine

To evaluate the effects of AI-based approaches in the identification, evaluation, and enhancement of marine bioactive compounds for cancer treatment, which encompasses techniques such as computational modeling, deep learning, and molecular docking.[19]

Investigation of AI-Driven Strategies to Overcome Drug Resistance

To investigate the potential of AI technologies in forecasting and addressing drug resistance through the analysis of genomic data from tumors, while also enhancing the use of marine-derived compounds in cancer types that exhibit resistance.[19,20]

Advancing AI-Guided Precision Drug Delivery of Marine Compounds

To assess how AI-driven nanotechnology and targeted delivery systems improve the bioavailability, stability, and tumor-targeting efficacy of anticancer agents sourced from marine organisms.[17,21-23]

Identifying Knowledge Gaps and Future Research Directions

To identify current shortcomings in the field of AI-based marine drug discovery, suggest potential research directions, and recommend methods to improve the clinical application of AI-enhanced marine bioactive therapies.[21,23]

METHODOLOGY

Search Strategy

A thorough literature review was performed utilizing PubMed, Web of Science, Scopus, and Google Scholar to find studies pertaining to bioactive compounds derived from marine sources that exhibit anticancer effects and their applications driven by artificial intelligence. The search incorporated various combinations of the following terms: "marine bioactive compounds AND cancer," "AI AND drug discovery AND marine natural products," "marine-derived anticancer agents AND precision drug delivery," and "AI AND cancer drug resistance AND marine compounds." Boolean operators (AND, OR) were employed to enhance the specificity of the search results. Only articles published in English-language peer-reviewed journals were included in this review.

Inclusion & Exclusion Criteria

Inclusion Criteria

Studies meeting the following criteria were included:

- AI-powered marine drug discovery studies, including *in silico* screening, machine learning, and deep learning models.
- Experimental and clinical studies on marine bioactives with documented anticancer properties.
- AI-driven drug delivery systems for marine-derived anticancer compounds.
- Cancer resistance studies investigating the role of marine bioactives in overcoming drug resistance.

Exclusion Criteria

Studies were excluded if they met any of the following conditions:

- Research on marine bioactives without cancer relevance.
- AI applications unrelated to oncology or marine-based therapeutics.
- Review articles without original data, meta-analyses, or opinion pieces.

Data Extraction & Analysis

Relevant data were extracted from each study using a standardized extraction form, including:

- Source of the bioactive compound (e.g., sea sponges, macroalgae, cyanobacteria, deep-sea bacteria).
- AI models used (e.g., machine learning, deep learning, Quantitative Structure-Activity Relationship [QSAR] modeling).
- Mechanism of action of marine bioactives (e.g., apoptosis induction, autophagy modulation, angiogenesis inhibition).
- Clinical translation stage (e.g., preclinical, clinical trials, FDA-approved therapies).
- AI-driven delivery methods (e.g., nanoparticles, liposomes, hydrogels) and their effectiveness in enhancing drug bioavailability and tumor targeting.

AI-DRIVEN MARINE BIOACTIVE DRUG DISCOVERY

Overview of Marine Bioactive Compounds in Cancer Therapy

Marine organisms generate a wide variety of bioactive substances that exhibit notable anticancer effects. Numerous compounds derived from these organisms possess distinct mechanisms of action, such as stabilizing microtubules, alkylating DNA, inhibiting proteasomes, and inducing apoptosis. The marine-derived compounds listed below have shown strong anticancer activity in both preclinical and clinical research (Figure 2):

- **Sea Sponges-Discodermolide:** A compound that stabilizes microtubules and demonstrates cytotoxic properties against lung, breast, and ovarian cancers. It shows synergistic effects when used with paclitaxel and may offer potential for addressing chemotherapy resistance.[24,25]
- **Tunicates-Ecteinascidin-743 (ET-743, Trabectedin):** A DNA alkylating compound that has received approval for use in treating soft tissue sarcoma and ovarian cancer. It promotes the formation of double-strand breaks in DNA and influences the tumor microenvironment.[26]
- **Deep-Sea Bacteria-Salinosporamide A:** A proteasome inhibitor obtained from Salinispora tropica, which demonstrates efficacy in treating multiple myeloma and presents potential as a viable option for malignancies that are resistant to bortezomib.[27]
- **Macroalgae-Fucoidan:** A sulfated polysaccharide derived from brown algae exhibits anti-angiogenic, apoptotic, and immunomodulatory properties in the context of liver and colorectal cancer. Additionally, it improves the effectiveness of chemotherapy.[26-28]
- **Marine Cyanobacteria-Curacin A:** A powerful cytotoxic agent that inhibits tubulin polymerization, demonstrating effectiveness against colon cancer and cancer cell lines resistant to multiple drugs.[9]

While these substances demonstrate significant anticancer effects, obstacles like limited bioavailability, inadequate solubility, and toxicity issues impede their progression to clinical use. The application of AI in drug discovery presents novel approaches to overcome these difficulties.

AI2 e these substances demonstrate

Artificial Intelligence (AI) has transformed the domain of drug discovery by hastening the processes of identifying, refining, and repurposing bioactive substances. Its significance is especially pronounced in marine-oriented drug discovery, where the extensive chemical variety found in marine life and the intricate methods involved in their extraction and evaluation present unique challenges. Methods utilizing AI encompass (Figure 3).

AI-Based Screening of Marine Bioactive Databases

AI is capable of swiftly assessing large collections of marine compounds, allowing for predictions regarding their bioactivity, toxicity, and drug-like properties. The use of neural networks and deep learning algorithms aids in identifying the most promising candidates for further experimental testing.[29,30]

Molecular Docking & Virtual Screening for Cancer Drug Targets

AI-driven molecular docking algorithms are capable of forecasting the interactions between marine bioactives and oncogenic targets, such as kinases, proteasomes, and microtubules.[31] Virtual screening markedly decreases both the time and expenses linked to conventional high-throughput screening techniques.[23,26,32]

AI-Driven Structural Modifications for Bioavailability & Potency Optimization

AI-assisted molecular design facilitates the alteration of compounds sourced from marine organisms to improve their pharmacokinetic properties and therapeutic effectiveness. Generative AI models forecast synthetic derivatives that possess better solubility and decreased toxicity.[33]

Machine Learning & QSAR Modeling to Predict Anticancer Properties

Quantitative Structure-Activity Relationship (QSAR) modeling employs artificial intelligence to recognize patterns for forecasting the effectiveness of marine compounds in relation to their molecular structures. Machine learning techniques are capable of discovering new marine bioactive substances that may work synergistically with current chemotherapy treatments.[30-33]

OVERCOMING CANCER DRUG RESISTANCE WITH MARINE BIOACTIVES & AI

Cancer Drug Resistance: Mechanisms & Challenges

Cancer drug resistance continues to pose significant challenges to successful treatment, resulting in both therapeutic failure and the recurrence of tumors. Various mechanisms play a role in this resistance (Figure 4), such as:

Multidrug Resistance (MDR) and Efflux Pumps

MDR is frequently facilitated by ATP-Binding Cassette (ABC) transporters, including P-glycoprotein (P-gp/ABCB1), Multidrug Resistance Protein 1 (MRP1/ABCC1), and Breast Cancer Resistance Protein (BCRP/ABCG2). These proteins function by actively expelling chemotherapeutic drugs from cancer cells, which leads to a decrease in the accumulation of these drugs within the cells.[34,35] The increased activity of these efflux pumps leads to the ineffectiveness of chemotherapy drugs like doxorubicin, paclitaxel, and cisplatin.[36]

Genetic Mutations and Adaptive Signaling Pathways

Mutations in critical oncogenes, such as TP53, KRAS, and BRAF, along with changes in tumor suppressor genes, modify how cells respond to treatment.[35-37] The stimulation of pro-survival signaling pathways, including PI3K/AKT/mTOR and MEK/ERK, contributes to drug resistance by inhibiting apoptosis and enhancing cell proliferation.[38]

Tumor Microenvironment (TME)-Induced Resistance

The Tumor Microenvironment (TME), which includes Cancer-Associated Fibroblasts (CAFs), immune cells, and the Extracellular Matrix (ECM), establishes conditions that are both hypoxic and immunosuppressive, thereby facilitating resistance to chemotherapy.[35,39] Tumor hypoxia results in the upregulation of HIF-1α, which modifies drug metabolism and enhances angiogenesis, ultimately diminishing the effectiveness of chemotherapy.[36,40]

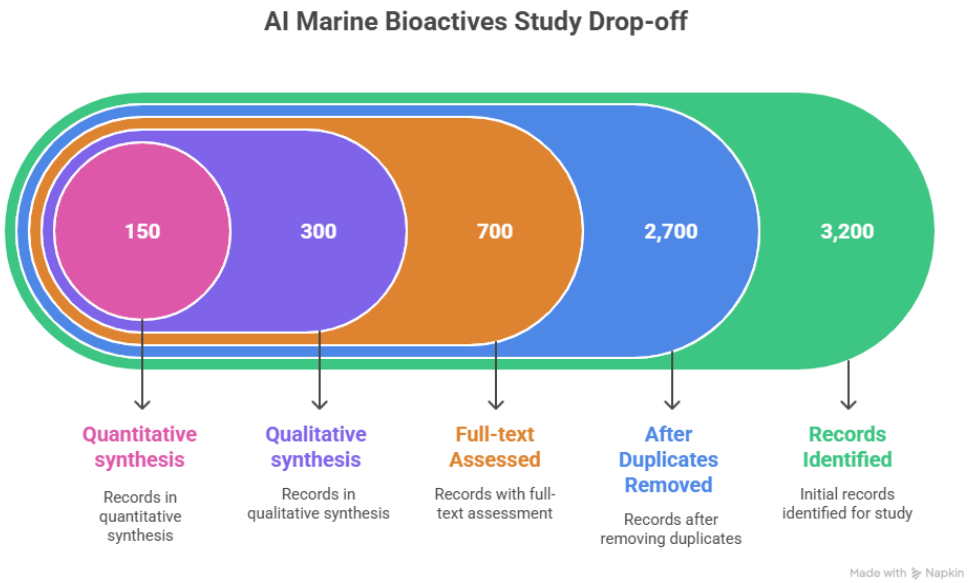

Figure 1: This PRISMA flow diagram.

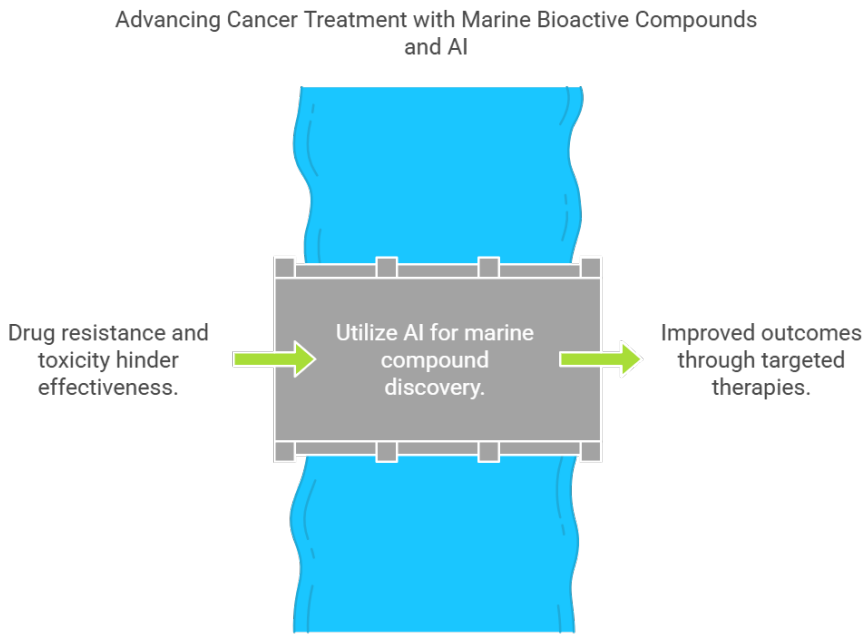

Figure 2: "AI-driven marine bioactive compound discovery for targeted cancer therapies".

Given these mechanisms of resistance, bioactive compounds derived from marine sources have surfaced as promising alternatives because of their distinctive capacity to influence tumor biology and counteract conventional chemoresistance.

Marine Bioactives Targeting Drug Resistance

- Marine bioactives demonstrate strong anticancer effects and have been shown to counteract resistance mechanisms via distinct molecular interactions. Notable compounds consist of:

Salinosporamide A: Overcomes Proteasome Inhibitor Resistance

Salinosporamide A, obtained from Salinispora tropica, serves as a strong inhibitor of the proteasome. It effectively addresses resistance to bortezomib in cases of multiple myeloma by permanently attaching to the 20S proteasome.[37-41] Unlike bortezomib, it demonstrates greater selectivity and reduced toxicity, positioning it as a potentially effective treatment for resistant cancers.[42]

Fucoidan: Modulates Cancer Stem Cells (CSCs) and MDR Proteins

Fucoidan, a sulfated polysaccharide derived from brown seaweeds, interferes with drug resistance by focusing on Cancer Stem Cells (CSCs), which are crucial in the processes of tumor relapse and resistance to chemotherapy.[35,36,39] It also suppresses the expression of P-glycoprotein (P-gp) and Multidrug Resistance Protein 1 (MRP1), leading to a decrease in drug efflux mediated by Multidrug Resistance (MDR).[36,38]

Ecteinascidin-743 (Trabectedin): Reverses Epigenetic Drug Resistance

Trabectedin, which is sourced from tunicates (*Ecteinascidia turbinata*), operates by influencing transcription factors and regulating epigenetic mechanisms.[36,37,39] It reestablishes sensitivity to chemotherapy by triggering breaks in DNA strands and inhibiting genes associated with resistance.[34-39]

These compounds sourced from marine environments present promising potential in addressing cancer drug resistance, especially when integrated with AI-enhanced strategies for precision oncology.

AI's Role in Predicting & Overcoming Drug Resistance

AI has become a significant asset in examining resistance trends, discovering new drug targets, and enhancing treatment strategies for tumors that are resistant.

AI-Driven Genomic Analysis to Detect Resistance Biomarkers

AI has the capability to examine extensive genomic datasets to pinpoint predictive biomarkers associated with drug resistance, such as mutations in TP53, alterations in ABC transporters, or epigenetic changes.[43] Machine learning algorithms can categorize tumors according to their responsiveness to compounds derived

from marine sources, aiding in the development of personalized treatment strategies.[44]

AI-Powered Drug Repurposing for Marine Bioactives Targeting MDR Tumors

AI algorithms, such as deep learning and molecular docking simulations, have the potential to repurpose bioactive compounds derived from marine sources for the treatment of resistant cancers by forecasting their binding affinities and interactions with drugs.[45] AI-powered computational models have successfully discovered fucoidan analogs that exhibit enhanced potential for inhibiting multidrug resistance, thereby improving treatment results.[46]

Deep Learning Models Predicting Tumor Microenvironment Adaptation

AI-enabled spatial transcriptomics and deep learning technologies can identify resistance mechanisms influenced by the Tumor Microenvironment (TME). This advancement paves the way for AI-optimized drug combinations that target Cancer-Associated Fibroblasts (CAFs) and pathways driven by hypoxia.[47] AI has the capability to forecast the combined effects of marine bioactives and Immune Checkpoint Inhibitors (ICIs) to address immune evasion.[45-47]

AI-GUIDED PRECISION DRUG DELIVERY OF MARINE-DERIVED CANCER THERAPIES

Challenges in Delivering Marine-Derived Anticancer Compounds

- Despite the potential anticancer benefits of bioactive compounds derived from marine sources, their application in clinical settings is obstructed by various pharmacokinetic and pharmacodynamic issues.

Poor Bioavailability

Many compounds derived from marine sources display limited solubility in water and poor absorption in the gastrointestinal tract, which decreases their overall bioavailability in the body.[48] Trabectedin, an effective anticancer compound sourced from marine organisms, experiences significant binding to plasma proteins, which restricts its concentration of free drug in the bloodstream.[49]

Rapid Metabolism and Short Half-Life

Some bioactive compounds derived from marine sources are quickly metabolized by the liver, resulting in brief half-lives and diminished therapeutic effectiveness.[50] Salinosporamide A, a strong proteasome inhibitor derived from deep-sea microorganisms, undergoes rapid hydrolysis in plasma, which requires the development of alternative methods for its delivery.[49,51]

Off-Target Toxicity and Drug Accumulation

Numerous marine bioactive compounds exhibit significant cytotoxic properties, potentially resulting in unintended off-target effects and overall systemic toxicity.[52] Fucoidan has shown hepatotoxic effects and immunomodulatory properties that depend on the dosage in preclinical research.[52,53]

AI-powered drug delivery systems present novel approaches to address these challenges by improving formulation design, increasing targeting efficiency for tumors, and reducing overall systemic toxicity.

AI-Powered Drug Delivery Strategies

AI has transformed precision oncology by enhancing the administration of anticancer agents sourced from marine environments. The combination of AI with nanotechnology,

Table 1: Comparative Toxicological Profile of *Peganum harmala* and *Cucurbita pepo* Based on Preclinical and Clinical Data.

Toxicological Parameter	*Peganum harmala* (PH)	*Cucurbita pepo* (CP)
LD_{50} (Oral, Rodents)	Harmaline: 300-500 mg/kg; crude extract: ~400-600 mg/kg.	>2000 mg/kg (no acute toxicity signs in rats/mice).
Neurotoxicity Risk	High doses may cause hallucinations, seizures, and coma.	No reported neurotoxic effects.
Hepatotoxicity	Increased liver enzymes and histopathological damage in animal studies.	No hepatotoxic effects noted even at high doses.
Serotonin Syndrome Potential	Significant risk; contraindicated with SSRIs, TCAs, MAOIs.	Minimal risk; theoretical involvement via tryptophan.
MAO-A Interaction Risk	Strong reversible inhibition by β-carbolines.	No direct MAO inhibition.
Dietary Safety Classification	Not classified as GRAS.	GRAS for food and supplements.
Clinical Case Reports	Multiple poisoning incidents linked to traditional use.	No known cases of clinical toxicity.
Drug-Drug Interaction (SSRIs, etc.)	Documented risk of serotonin syndrome.	No adverse interactions reported.
Allergenicity	Rare, non-specific hypersensitivity.	Rare sensitivity to pumpkin seeds.
CNS Penetration and Accumulation	Lipophilic β-carbolines cross BBB; accumulate in CNS and liver.	Some lipophilic antioxidants may cross BBB.

hydrogels, and bioprinting has markedly increased the effectiveness of drug delivery.

Nanoparticle-Based Delivery (AI-Optimized Liposomes, Micelles)

AI-powered models are capable of forecasting the ideal dimensions, configuration, and surface properties of nanoparticles to improve their ability to penetrate tumors and be absorbed by cells.[54] Liposomes and polymeric micelles, optimized through AI techniques, are capable of encapsulating compounds sourced from marine environments, thereby enhancing their stability and bioavailability.[50,54] AI-enhanced fucoidan-loaded nanoparticles have shown improved tumor retention and decreased off-target toxicity in models of hepatocellular carcinoma.[54,55]

Hydrogel Formulations for Localized Delivery

AI-enhanced hydrogels facilitate the prolonged and targeted delivery of bioactive compounds sourced from marine organisms, thereby minimizing systemic adverse effects.[56] AI algorithms forecast the time required for gelation, the rate of degradation, and the kinetics of drug release, thereby facilitating a regulated release at tumor locations.[55-57] Trabectedin-encapsulated hydrogels have demonstrated extended retention in sarcoma models, leading to a decrease in dosing frequency and an enhancement in therapeutic effectiveness.[58]

AI-Assisted Bioprinting of Personalized Drug Carriers

AI-supported three-dimensional bioprinting facilitates the creation of personalized drug delivery systems tailored to individual patients, enhancing the release dynamics of marine bioactive compounds.[50,51,53] AI-driven bioprinted frameworks are capable of delivering marine-sourced anticancer compounds in reaction to stimuli from the tumor microenvironment, such as pH changes and hypoxia.[53,57]

Machine Learning to Enhance Tumor-Targeting Efficiency

AI-powered machine learning algorithms examine the variability within tumors to determine the most effective drug delivery method tailored to each patient.[50,56-58] AI models that have been developed using pharmacokinetics and biodistribution information can enhance the surface functionalization of nanoparticles to better target tumors.[48,58] AI-powered simulations have shown improved accuracy in targeting marine bioactive-loaded nanocarriers, leading to decreased systemic clearance and heightened tumor accumulation.[48,55]

FUTURE DIRECTIONS & RESEARCH GAPS

Expanding AI-Driven Marine Bioactive Databases

The identification of bioactive compounds from marine sources for cancer treatment is constrained by the absence of extensive AI-driven screening datasets. Despite the ocean's vast chemical diversity, only a small portion of its bioactive substances has been discovered and researched.[59] The combination of machine learning and deep learning frameworks with marine compound databases is essential to:

Create AI-Driven Marine Compound Repositories

Current datasets in marine pharmacology are insufficient and lack proper annotations, which hinders the capability of AI to forecast anticancer effects, toxicity levels, and bioavailability.[60] AI-based screening databases, akin to ZINC and ChEMBL for

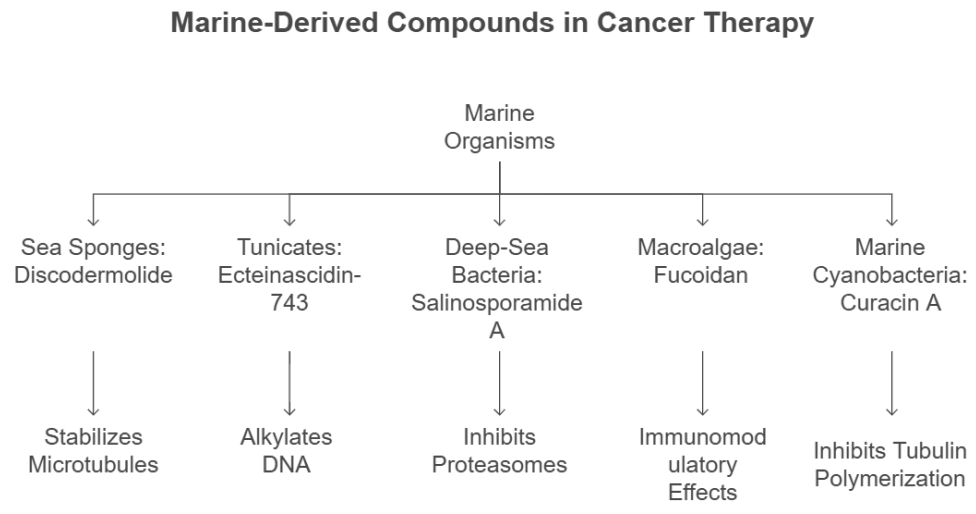

Figure 3: "Marine-derived compounds in cancer therapy: bioactive molecules from marine organisms targeting microtubules, DNA, proteasomes, immune modulation, and tubulin polymerization".

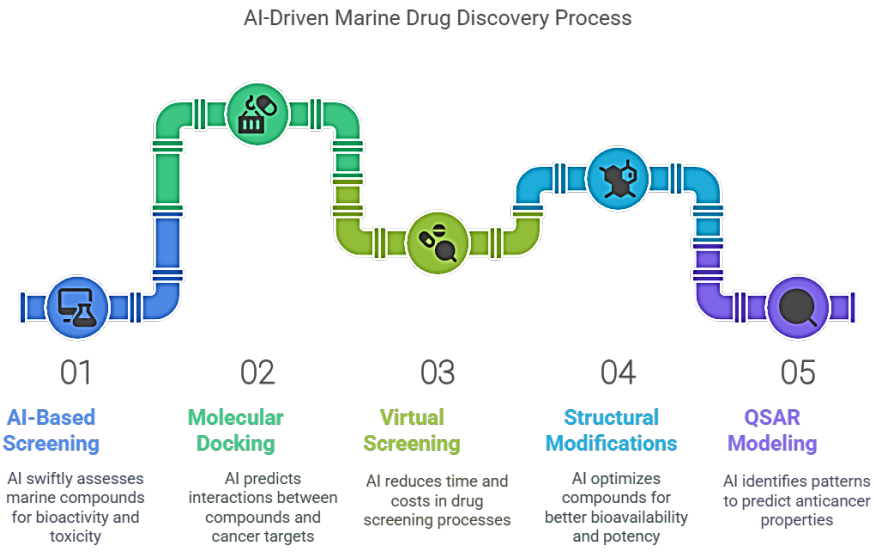

Figure 4: AI-driven marine drug discovery: screening, docking, virtual screening, structural modifications, and QSAR modeling for anticancer compounds.

synthetic pharmaceuticals, must be developed specifically for marine bioactive compounds.[59, 61]

Develop AI-Guided Sustainable Marine Bioprospecting

Uncontrolled marine bioprospecting presents a risk to biodiversity, especially in deep-sea ecosystems.[58,62]AI models are capable of forecasting marine species that possess significant bioactive potential, thereby reducing unnecessary harvesting and facilitating environmentally sustainable sourcing of compounds.[62,63]AI-driven synthetic biology can additionally aid in the laboratory production of compounds derived from marine sources, minimizing environmental effects.[56,63]

Without the utilization of AI-driven methods, numerous potentially revolutionary anticancer agents derived from marine sources might go unnoticed because of the immense complexity involved in screening the extensive biodiversity found in marine environments.

AI-Optimized Drug Formulations for Clinical Translation

Although artificial intelligence has greatly advanced the identification of marine bioactives, a considerable disparity persists between AI predictions made *in silico* and their validation through *in vivo* studies. Important avenues for future research encompass:

Bridging the Gap Between AI Predictions & Experimental Validation

Many marine bioactives identified through AI predictions do not successfully convert into effective *in vivo* treatments, often due to issues related to stability, solubility, or pharmacokinetics.[64] AI-powered multi-scale modeling has the capability to combine molecular docking, predictions related to ADMET (Absorption, Distribution, Metabolism, Excretion, Toxicity), and real-world pharmacokinetic data to enhance the dependability of *in silico* results.[65] AI-enhanced CRISPR gene editing could facilitate the synthetic generation of uncommon bioactive compounds derived from marine sources, exhibiting enhanced clinical characteristics.[66]

AI's Role in Real-Time Monitoring of Patient Response to Marine-Based Drugs

AI-based identification of biomarkers has the potential to forecast how patients will respond to marine bioactives in tailored cancer treatments.[62,64] Machine learning algorithms have the capability to evaluate changes in the tumor microenvironment, alterations in metabolism, and immune system reactions, thereby facilitating real-time optimization of dosage modifications.[48,62,66] AI-powered wearable biosensors and liquid biopsy methods could facilitate ongoing assessment of the effectiveness and safety of medications in individuals undergoing cancer treatment.[59,61,64]

Without the enhancements provided by AI, the clinical application of anticancer agents derived from marine sources is likely to continue at a sluggish and uncertain pace.

Ethical & Sustainability Considerations

While bioactive compounds sourced from marine life show potential for cancer treatment, it is essential to tackle ethical issues and sustainability challenges prior to their widespread implementation. Important areas for upcoming research encompass:

AI-Driven Synthetic Marine Analogs to Avoid Overharvesting

Overexploitation of marine organisms for pharmaceutical purposes presents a significant environmental threat.[67] AI-supported synthetic biology and bioengineering have the capability to produce marine-derived analogs in controlled laboratory environments, thereby safeguarding biodiversity.[68] AI-powered fermentation and metabolic engineering techniques are currently employed to produce Trabectedin (derived from tunicates) and Salinosporamide A (extracted from deep-sea bacteria) independently of natural sources.[69]

Regulatory Challenges in Marine-Derived AI-Based Drug Approvals

The process for regulating marine bioactives identified through artificial intelligence is still ambiguous, as existing drug approval systems were established with conventional drug development in mind.[70] AI-based drug discovery is required to comply with stringent validation criteria established by the FDA, EMA, and WHO. This creates a need for the formulation of new regulatory frameworks specifically for AI-enhanced marine pharmaceutical candidates.[71] Ethical issues regarding AI bias in drug screening, the ownership of data, and the safeguarding of indigenous marine knowledge need to be taken into consideration as well.[72]

CONCLUSION

Artificial Intelligence (AI) is transforming the process of discovering and clinically translating anticancer medications sourced from marine organisms by enhancing the identification of bioactive compounds, streamlining molecular optimization, and improving precision in drug delivery.[29] The extensive variety of life forms within marine ecosystems yields a wealth of structurally distinct bioactive compounds, many of which demonstrate strong anticancer effects. Nonetheless, issues such as low bioavailability, resistance to multiple drugs, and pharmacokinetic obstacles have traditionally hindered their use in clinical settings. Approaches driven by artificial intelligence are tackling these issues by allowing for *in silico* screening, predictive modeling, and real-time monitoring of patient responses, thereby enhancing the potential for personalized cancer treatment.[73,74]

Marine-derived substances like Salinosporamide A, Fucoidan, and Trabectedin present novel approaches to address drug resistance by focusing on cancer stem cells, epigenetic modifiers, and the mechanisms of multidrug efflux.[72,73,75] The incorporation of AI-driven machine learning models and deep learning techniques improves the capacity to forecast drug interactions, fine-tune dosing approaches, and enhance synergistic combinations with current chemotherapy treatments.[65,69,70,73,75] AI-powered precise drug delivery mechanisms, such as nanoparticles, liposomes, hydrogels, and AI-enhanced bioprinting, enhance the targeting of tumors, minimize off-target toxicity, and boost therapeutic effectiveness.[62,64,65,68,72,73]

Despite these progressions, there remains a pressing requirement for extensive AI models capable of predicting, optimizing, and sustainably providing therapies derived from marine sources. Establishing AI-focused marine pharmacology databases will be essential for improving drug discovery processes and facilitating regulatory approvals.[65,67,72] Furthermore, synthetic biology and metabolic engineering enhanced by AI present promising solutions to the excessive harvesting of marine species, thereby promoting the responsible and sustainable generation of marine bioactive compounds.[64,67,69,71,75]

By combining artificial intelligence with marine pharmacology, the development of cancer drugs can be notably expedited. This integration helps to decrease toxicity levels, enhance treatment results, and support precision medicine strategies. Future studies should aim to broaden AI-curated libraries of marine bioactive compounds, improve predictive models for clinical use, and create clear regulatory guidelines that ensure the safe and effective implementation of marine-derived anticancer treatments in clinical settings (Table 1).[63,67,69,73]

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

AI: Artificial Intelligence; **MDR:** Multidrug Resistance; **PRISMA:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses; **DNA:** Deoxyribonucleic Acid; **RNA:** Ribonucleic Acid; **VEGF:** Vascular Endothelial Growth Factor; **EAS:** External Anal Sphincter; **IAS:** Internal Anal Sphincter; **CSCs:** Cancer Stem Cells; **DDR:** DNA Damage Response; **EPIs:** Efflux Pump Inhibitors; **MRSA:** Methicillin-Resistant Staphylococcus aureus; **mVOCs:** Microbial Volatile Organic Compounds; **ML:** Machine Learning; **DL:** Deep Learning; **RND:** Resistance Nodulation Division; **MFS:** Major Facilitator Superfamily.

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