MARINE ALKALOID: CURRENT STATUS AND FUTURE PROSPECTS IN DRUG DISCOVERY

Zia Ur Rehman *Panizai[1], Yousaf Khan[2], Bashir Ahmed [3]*

[1]: Department of Chemistry, University of Baluchistan, Quetta.

[2]: Department of Chemistry, COMSATS University Islamabad campus, 45550, Islamabad.

[3]: Department of microbiology Quaid e Azam university Islamabad Pakistan

ABSTRACT

A variety of diseases can be treated with marine natural products traditionally. Drug discovery and drug development have been greatly facilitated by these marine alkaloids. Various minerals, plants, microbes, and animals are used to extract these marine natural products. Biological diversity is greatly influenced by these marine natural alkaloids. In the near future, a large number of compounds are being tested in clinical trials that have been extracted from marine plants and animals. As a source of therapeutic agents, marine alkaloids are considered as being of medicinal importance in the pharmaceutical industry. It has been discovered that many potent molecules are capable of preventing cancer, viral, inflammatory, and microbial diseases. Hence, it is necessary to explore these marine alkaloids now and in the near future to design, develop, and discover new drugs.

1. INTRODUCTION

The largest number of alkaloid compounds is from marine species. As a polyoxygenated dihydropyrano[2,3-c]pyrrole-4,5-dione derivative, pyranonigrin A and F, were isolated from the endophytic fungus penicillium brocae MA-231. These compounds exhibit a wide range of antimicrobial activities against human and plant pathogens [1]. Indole diketopiperazine spotted through culture extract of *Eurotium cristatum* has high microbial activities but rubrumazine B shows medium against plant pathogenic fungus. Echinulin, dehydroechinulin, and variecolorin H possess light microbial activities against human pathogen *s.aureus*. Thus, the supposition is made that indole diketopiperazine alkaloids obtained from tryptophan residue with a second amino acid as L-alanine possess low antimicrobial activity [2]. Echinulin, cristatumin D, and

tardioxopiperazine A can't hamper the extension of plant-pathogenic fungi, *alternaria brassicae, valsa mali, physalospora obtuse, alternaria solania*, and *sclerotinia miyabeana* but active against *escherichia coli* and *s.aureus* bacteria. Antibacterial activity of cristatumin A is the same as serine residue in the 2,5-diketopiperazine moiety and as compared to neoechinulin A has alanine residue. Changes between the structure of isoechinulin A and tardioxopiperazine A are at C-8/C-9 i.e tardioxopiperazine A has the single bond between C-8/C-9 which is necessary for its antibacterial activity [3]. Antimicrobial activity against *e.coli* and *c.albicans* is shown by hemimycalins A and B which are N-alkylated hydantoin alkaloids separated from the Red Sea sponge but these are inert to *s.aureus* [4]. In China dithiodiketopiperazine derivative peniciadametizine A and its similar peniciadametizine B were separated from penicillium adametzioides AS-53 that was obtained from a marine sponge. The above compounds are inert to bacteria and plant-pathogenic fungi but show activities against *a. brassicae* [5]. Penicibrocazines A and E derivatives of antimicrobial sulfide diketopiperazine separated from culture extract of Penicillium brocae MA-231 is an endophytic fungus obtained from the fresh tissue of the marine mangrove plant Avicennia. The compounds Penicibrocazines B and E are inert to *eromonas hydrophilia, e.coli, v. harveyi, V. parahaemolyticus,* and the plant-pathogenic fungi, *A. brassicae, Colletotrichum gloeosporioides* and *Fusarium graminearum* but active against human, aquatic and plant-pathogenic microbes including *s.aureus, micrococcus luteus, and gaeumannomyces graminis.*

Due to the double bond at C-6 and C-60 penicibrocazine A is active against *s.aureus* but peniciadametizine C is not. It was inert to microorganisms but all this was due to a double bond at C-6 and C-60. Penicibrocazine D has strong activity against *G. graminis* because of its s-methyl groups and peniciadametizine E has antimicrobial activity because of the keto group at C-5/50 as compared to peniciadametizine A [6]. Crambescidin 800 shows resistance to the activity of *acinetobacter baumannii* that is separated from the sponge *clathria cervicornis* [7]. An alkaloid isolated named xinghaiamine A was separated from marine fungus *actinomycete streptomyces xinghaiensis.* It shows antibacterial activities against gram-negative and gram-positive pathogens microbes on a broad spectrum. These microbes show resistance to drugs but xinghaiamine is effective against them. Against *c.albicans* it does not demonstrate any antifungal activity. Biological activities like antimicrobial activities represent a broad spectrum of sulphoxide element present in xinghaiamine A [8]. A specie named trios is Red Sea Sponge, which gives hyrtioerectines D and F. It is possible through bioassay fraction performed on ethyl acetate portion

extracted from hyrtios. They show antimicrobial activities against S. aureus but are inert to *E.coli*. The di-phenolic element present in them is responsible for higher antimicrobial activities. Acetamide is responsible for mild activity in hyrtioerectines F. In the South China Sea, marine sponge sources like *Agelas mauritiana* were used to obtain ageloxime B and D. These are diterpene alkaloids and show antimicrobial activity against S. aureus and retard the growth of C.neoformans [9]. Zamamidine D is a manzamine alkaloid. It has a 2,20-methylenebistryptamine structure in it. In it, β-carboline is replaced with an aromatic part that is effective against bacteria and fungi. Zamamidine D is separated from marine species named Okinawan Amphimedon [10]. The derivatives of bisthiodiketopiperazine are obtained from marine sponge fungus that is adametzioides AS-53. The derivatives adametizines A and B are different from each other by the presence of the Chlorine group and a hydroxyl group at carbon-7 respectively. Adametizines A shows better antibacterial activity ty than Adametizines B [11]. In China, diterpene alkaloids are obtained from a marine sponge. These alkaloids show antimicrobial activities against microbes such as *c. albicans* and *e. coli*. These alkaloids are named Iso-agelasidine B and C and are used for antifungal activities against *c. albicans* and slightly retard the growth of bacteria. Diterpene alkaloids like iso-agelasine C agelasine B and J show antifungal activities. All these contain a 9-N-methyladeninium part. Brevianamide F shows antimicrobial activity against *S.aureus* and anti-fungal activities against *C.albicans*. It is separated from Penicillium vinaceum which is a marine fungus [12]. From the Arctic Ocean a secondary metabolite is obtained that has antifungal activity against *C. albicans*. It is N-(2-hydroxyphenyl)-2-phenazinamine obtained from Nocardia dassonvillei [13]. There are various marine alkaloids and their sources are summarized in figure 1.

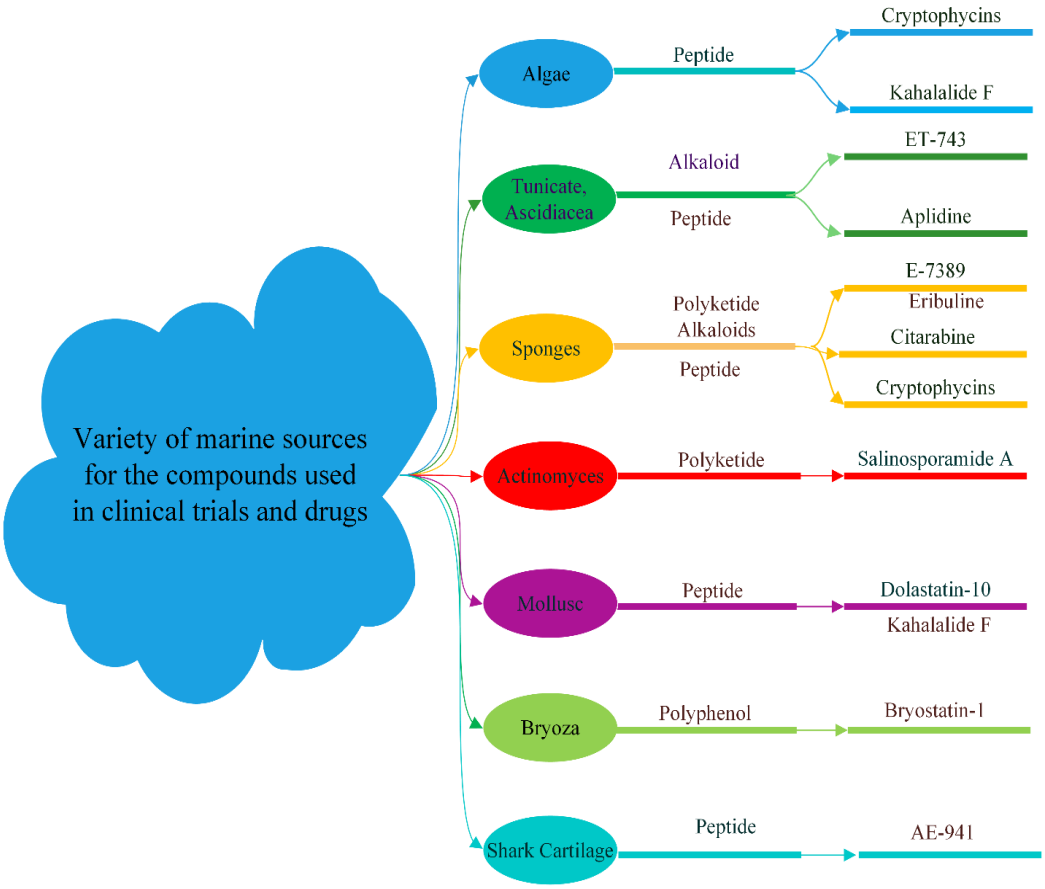

Figure 1. Clinical trials of various marine sources in drug discovery

2. CONCLUSION

Marine alkaloids have potential as pharmacological agents. It is due to the diversity of their structures that these marine alkaloids are of therapeutic importance. A limited accessibility of the deep sea has posed challenges to researchers in exploring marine alkaloids. It is mainly used for treating cancer diseases with these marine alkaloids. The active constituents derived from these marine animals will synergistically combine with herbal ingredients showing significant therapeutic activity. Thus, it is essential to study marine alkaloids for their anti-tumor, anti-inflammatory, anticancer, and anti-microbial properties. Marine alkaloids have bright industrial applications and will play a significant role in the prevention of various diseases in the near future. Future drug discovery will be based on these marine alkaloids' clinical development. Marine

alkaloids would be evaluated, spectroscopically characterized, and molecular docking would be conducted to assist in drug discovery. In conclusion, the family of marine alkaloids will be helpful in finding new potent molecules for the eradication of the disease.

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