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Article

# Re-emphasizing the diversity and relevance of chitosan-nano-types derived from marine-actinomycetes; a biotechnological and industrialization blueprint

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**Abstract:** One emerging and novel area of biotechnology is the application of microorganisms, their biochemical products and other additional bio-molecules for human, animals and plant livelihood improvements. Such areas of growing scientific strides are made principally by the understanding of genomics (or metagenomics), proteomics and culturonomics, as it is recently advancing especially among biopolymers sourced from marine niche. One such bio-molecule recovered from marine habitats is chitosan and its nano-type derivatives from marine organisms (Actinomycetes). The study describes re-emphasizing the diversity and relevance of chitosan-nano-types derived from marine-actinomycetes; a biotechnological and industrialization blueprint. A title-based search was applied to collate relevant documents from the Scopus database, PubMed database, and Web of Science (WoS) database using a Boolean previously described by related investigators. Eligible data sets on chitosan-nano particulate were screened and used to describe/evaluate diverse research-based and knowledge-scape of marine-based nanochitosan. Emphasis revealed the biodegradability, biocompatibility, high adsorbent and versatility with increased selectivity in stain/dye removal as well as metallic-pollutant/organic-waste removal, inexpensiveness and environmental friendliness. It is hoped that the biomolecular versatility, biocompatibility, polycationic and nontoxic nature of nanochitosan from marine organism, may be applied as nano-type quaternized chitosan (QNC). A scientific mechanism that depends on charged molecules and targets, which may be directed at positively charged quaternary groups, nucleic acids (DNA and RNA), proteins/amino acids, hydroxyl and carboxylic ions. Such advancement would give birth to a new approach to scientific research, improve molecular studies, biotechnological processes, pharmaceutical companies, diagnostics/medicine, and also revolutionize industrialization.

**Keywords:** chitosan; nano-type; actinomycetes; nano-type quaternized chitosan; biotechnology; industrialization

## 1. Introduction

Globally, more than 140 million tons of biopolymers are synthesized annually with stable degradative potential and diverse bioactive capabilities. One notable biopolymer that has received major scientific interest is chitosan, which is formed from a partial deacetylation of chitin. It is naturally scavenged commercially from crustacean shells (e.g., lobsters, crabs, krill, squids, crawfishs and shrimps) by chemical deacetylation [1,2]. Chitosan is a biopolymer that consists of dual glucose subunits, N-acetyl-D-glucosamine (GlcNAc) and D-glucosamine (GlcN), that are cross-linked with a β(1→4) glycosidic bonds and distributed randomly. It is a natural, nonhazardous bio-molecule (biopolymer) that is produced commercially by the incomplete removal of the acetyl group from chitin. It is one such carbon derivative (or polymer) of interest that has shown multifaceted relevance in the field of science. Chitosan's multifaceted and diverse applicability is traceable to the polycationic and nontoxic nature of the polysaccharide subunits (cross-linked D-glucosamine and N-acetyl-D-glucosamine). Chitin, a parent source of chitosan is one of the most abundant natural biopolymers next to cellulose which is sourced from diverse organisms in crystallized microfibrils of their exoskeleton the cell wall of fungus, yeast and arthropods. Its pure form is extracted from the organismal exoskeleton by chemical (acid and alkaline) treatment and depigmentation [3]. However, the natural source of chitin has been greeted with limited industrial acceptability due to extraction demerits, impurity, stability, and other metallic contamination which affects or impacts the relevance of the biopolymer in diverse disciplines. According to the study of Younes and Rinaudo [3], the chemical extraction process results in physicochemical harm to chitin properties which leads to a decrease in Dalton/molecular weight and affects the intrinsic properties of pure chitin. It has also resulted high cost of obtaining pure chitin; affecting other chemical waste release when applied in wastewater treatment. The avoidance of such a chemical purification process promises a future for the sustainability of chitosan molecules as it would eliminate the various concerns of chemical extraction. In recent times, the knowledge of 'green chemistry' has gained interest in scientific advancement as it serves as a corrective measure for avoiding chemical extraction and the implementation of microbial protease (enzyme)-dependent extraction processes. Suffice it to say that the green chemistry approach employs the use of microbial enzymes for the extraction/purification of chitin. It is to this end the study determines the necessity of re-emphasizing the diversity and relevance of chitosan-nano-types derived from marine actinomycetes: a biotechnological and industrialization blueprint.

## 2. Materials and methods applied for data collection

### 2.1. Method of data collection

Relevant related documents from the Scopus database, PubMed database, and Web of Science (WoS) database were collated, and core data sets were screened for eligibility based on documents that were published on chitosan-nano particulate, their characteristics, source, and relevance in the control of bacterial infections and strategy of therapeutic application based on antimicrobial approach [4–7].

### 2.2. Strategy of search

Three electronic search databases were sourced which include the Scopus database, the PubMed database, and the Web of Knowledge (WoS), for previously published details on nano-chitosan since the last thirty years on 14 December 2024; 12.08 GMT + 2. A title-based search was applied during the study using the Boolean as previously described by various related investigators [8–10].

## 3. Results and discussion

Recovered/screened details and documents emphasized various aspects of biotechnology as well as other areas of scientific relevance of marine-based nano-chitosan which were discussed in sections including marine exploration for relevant bio-molecules, marine actinomycetes as potential sources of such bio-molecules, approaches to the exploration of such marine actinomycetes. These approaches may include the fermento-cultural approach, post-cultural and non-cultural genomics, and in Insilico-biomolecular targets. The study also emphasized chitosan and its derivatives especially in nano-based technologies as well as the diversity of their applications (application of nanochitosan) in animal husbandry, aquaculture and aquaponics, food preservation and conservation and other related areas. Some of the screened documents also discussed the problems of exploiting nanochitosan-based biopolymers and the global knowledge gap in their marine-derived type, the various marine microbes (actinomycetes)-derived members, their potential future prospects and their relevance. These fragmented sections were employed/applied in discussing the necessity of re-emphasizing the diversity and relevance of chitosan-nano-types derived from marine actinomycetes: a biotechnological and industrialization blueprint. Such an applicable green chemistry approach has revealed advantageous prospects as revealed by some related investigators' comparative study [11]. Some of the studies affirmed the state of chemical/biological extraction processes and the potential prospects of nano-based chitosan. It reported that chitin bio-extraction products were improved, preserved with high molecular potency, easy to manipulate, highly reproducible, lower in energy input, reduced in time to obtain components, and smaller in solvent consumption [11,12]. The previous works of Guerrero Legarreta et al. [13] and Cira et al. [14] has further contributed to green chemistry when they reported the relevance of lactic acid bacterial fermentation in the bio-transformation of chitin. However, the use of bacterial enzymes has been limited to studies of laboratory scale with most investigators of related studies directed towards laboratory investigation for chitin bio-extraction/bio-transformation [15,16]. Although the application of proteolytic enzymes to digest macro-compounds and/or fermentation processes using relevant microorganisms has been faced with the laboratory-scale limitation, it did not hinder the scientific progress in the area of chitosan studies; rather, it further advanced with a view to exploiting the relevance of chitosan especially in the areas of animal husbandry, aquaculture and food conservation. This has necessitated the exploration of microbial source chitosan and its improved relevance. According to the study of Akila [1], the fermentation product (mycelial wastes) of some fungi members poses potential for a stable non-seasonal chitosan source and/or raw material which is characterized by increased consistency and high quality.

In another development, nanotechnology which is seen as a science that emphasizes the control and manipulation of material masses in a nano-scale (109 nm) range with the special interest of improving life expectancy [17–19]. It is the diversity, multi-relevant capability of knowledge of chitosan in synergy with nano-technological advances that has today birthed the term nanochitosan. Nanochitosan, a term that is currently emerging, trending and gaining attention in various scientific disciplines has been characterized with polymeric carbon derivatives and nanotechnological dynamics. Such marriage between carbon derivatives, biopolymers and nanotechnology has been involved in fundamental technological applications including chemical industries, food industries and pharmaceutical companies. Another area where nanochitosan applicability has gained relevance is animal husbandry, aquaponics (recirculating aquaculture and hydroponics), and food conservation which are recently growing with specific interest in the area of study.

Animal husbandry which involves the science of animal breeding, and management has generated attention as the administration of vaccines helps to avoid the spread of infections and poor farm yield [20]. Using chitosan-succinate as an adjuvant poses control relevance for such animal necro-bacteriosis as the solution of chitosan-succinate may serve as a protective agent for drying, during the production of bovine rhinotracheitis vaccine and improves the immunogenic activities. In the area of aquaponics, which are systems that involve increasing economic and sustainable indoor and outdoor fish farming with improved efficiency both in farm health and productivity. Chitosan is added in combination with aquaponics (aquaculture with hydroponics) to obtain a novel study area called aquaponic-chitosan. Food conservation is another aspect where chitosan is applied to introduce hydrophobic groups and coating capsules to enhance food physiological features. Although the relevance of naturally sourced chitosan in the improvement of life expectancy and science remains endless, the microbially sourced by-products have promised a better future for studies on chitosan. Exploring the marine habitat has also revealed the extreme biodiversity of marine-based organisms due to the inhospitable nature of life in the marine environment [21]. This is an indication that microbial strains from the marine environment would possess the tendency for the production of better chitosan and derivatives, which, when combined with nanotechnology would present an advanced applicability of such products.

## 3.1. Marine exploration for biomolecules

Globally, the marine niche constitutes more than 90% of inhabitable space and it's the largest reservoir of life and forms on planet Earth. Although inhabitable space is large, life in the marine environment including the various existing animal phyla has only occupied about 80% of the ocean bed. The marine environmental niche has over time been a potential subject for exploration of diverse biomolecules due to the extreme conditions observed in the environment including low/high temperatures, low pH, high pressure, increased concentration of salt, etc. Such exploration activities have been shown to include the discovery of life and forms in the marine environment, deep-sea hydrothermal vent discovery, marine high hydropower in addition to exploration of novel bio-diverse microorganisms [22]. In the early discovery of marine microorganisms, following a comparative study, an extreme biodiversity of characteristics was observed amongst marine organisms of similar identity (kingdom, family, genera and species) with organisms from other habitat [22,23]. Members of organisms that were isolated from marine environments include halophile, thermophile, piezophile, polyextremophile, psychrophile as well as alkalophiles [24]. These organisms are exemplified as extremophilic organisms which possess extreme capability to thrive in characteristically high (Thermophiles) or low temperatures (Psycrophiles). Some of them thrive in high ionic strength (Halophiles) conditions, anaerobic conditions (Anaerobe), acid and/or alkaline pH (acidophiles, alkalophiles), high ultraviolet (UV) radiations, high pressures (Piezophiles) and other poly-extremophiles such as asthermo-acidophilic and thermo-halophilic organisms. In addition, some deep-sea habitats (piezosphere: depth greater than 1000 m), where the pressure is a little above 10 MPa, and the temperature is as low as 2–3 ℃ or as hot as 400 ℃ and more, as seen in the hydrothermal vents, thermo-piezophilic organisms and psychro-piezophilic organisms may also be found respectively [25]. Some of these marine organisms or extremophiles thrive also in salty water niches; hence their bio-products (biopolymers, lipids, enzymes) are presumed to possess unique features [19,26]. The organisimal diversity is based on their diverse cellular metabolic mechanisms and their ability to survive in extreme condition. These capabilities have impacted the potential for the utilization and/or breakdown of higher carbon atoms, multiple nutrient sources and the production of diverse bio-molecules of a broader spectrum. These biomolecules are numerous, novel and possess improved features including polymers, osmolytes and enzymes recovered from the marine microbial community. In addition, it has also been reported that these molecules of interest are currently receiving a growing need in several industrial production processes including the pharmaceutical, medical, environmental and food industries. Although, recent genomic studies have enhanced the exploration strategies, man’s existence has not been separated from exploration/disparate search for knowledge and the desire to understand the world around him. Man’s careful observation, movement (locomotion) and thinking ability were driving forces unto the acquisition of information around him. It was this quest that necessitated the term “forms and features”, which later developed into classifying living organisms in groups (Domain) known to be Bacteria, Archeae and Eukarya. It is clear that growth, development and advancement of knowledge originated the term Taxonomy, which is a branch of science saddled with the classification of organisms based on their evolutionary relationships [27,28]. Bacterial, one of the members in the classification of living organisms, are said to be prokaryotes which are simple unicellular but complexly organized organisms. Because the existence of these microbes is ubiquitous, they are found in diverse environments, making the marine environment a susceptible subject.

Life in the deep sea or marine demands adaptation to a range of extremely high pressure (approx: 1100 atmospheres), capnophilic conditions, low temperatures below 4 °C on the deep-sea level (which occur mostly within major global regions of Europe, America, Africa Asia etc.), a low pH value of 2.8 and high hydrothermal temperature at the mid-ocean region. It is reported that 67% of all bioactive compounds from marine bacteria are sourced in the Caribbean, Japan, the Indian Ocean, the western Pacific Ocean, Australia and the Mediterranean [29].

The above has shown that exploring the marine habitat possesses a potential for isolation of bacteria strains with extraordinary biodiversity due to their extreme exposure and extreme environmental features. Suffice it to say that over 70% of the Earth’s land surface area is covered by oceans and it is said that life on planet Earth originates from combining molecules at sea. Such extreme conditions in the marine environment have been estimated by experts to result in notably higher biodiversity in marine ecosystems (especially the deep-sea floor or coral reefs), when compared with those of the tropical rainforests [30]. This difference in environmental conditions in marine as compared to their terrestrial counterparts would necessitate a possibility for the bacteria members that thrive in such conditions to exhibit different characteristics from their terrestrial counterparts; hence, they may produce different types of bioactive subunits as well as secondary metabolites. From the forgoing, interest directed towards the discovery of marine microbes such as marine actinomycetes (and their bioproducts) has an inclination to result in the discovery of novel bioactive agents that will combat several human-related concerns. In an additional study, it was also reported that the development of microbial products has empowered applied combinatorial chemistry with secondary metabolites ranging from glycopeptides, alkaloids, polyketides, terpenoids and steroids. Presently over 23 microbial metabolite-derived active compounds have been launched in the markets of Europe, the United States and Japan from 2001–2005 [31]. Furthermore, over 136 microbial products and microbial-derived biomolecules are currently undergoing trial in major disciplines [31].

Following the observation of numerous bio-diverse microorganisms, their thriving tendency, and their distribution in the marine environments, various investigators of environmental studies have indicated research interest because of the increasing potential of such organisms. It is reported that such marine microorganisms posses relevance for the improvement of biogeochemical industries, environmental health sustainability activities, agricultural advancement and large-scale production, pollution control and environmental remediation, public health systems revamping, growth of food industries, advancement of pharmaceutical companies, innovation and activation of bio-catalyst companies and biotechnological industries [19,25,26,32].With growth and development in the aforementioned area, various investigators of marine studies seek ways of harnessing the potential of these marine-based bacteria for prolific production of numerous bio-molecules to enhance man's life [26,32].

### 3.2. Marine actinomycetes as sources of biomolecules

Dating back to the observation of life and forms in the marine environment, various groups of organisms have been reported by numerous investigators including protozoan, bacteria, viruses, fungi, etc. Although these groups of organisms are similar in characteristic to their progenies in other habitats, their extreme features and biodiversity have informed the marine habitat members to be grouped differently as follows: marine bacteria, marine fungi, marine protozoa, etc. Amongst the bacterial members is a group classified as actinomycetes, which are Gram-positive and possess the potential to survive in harsh environmental conditions [33]. These members of bacteria have been reported both in terrestrial and marine environments including swamp, debris, dump-sites and waste. Their observation in the marine has opened another area of study in bacteriology known as action-bacteriology. Marine action-bacteriology is a re-emerging area of scientific research both in the tropics and other regions of the world because of the economic, biotechnological, and pharmaceutical value of this group of microbes. These groups of organism are divided into 10 major divisions which comprise Gram-positive bacteria to which actinobacteria belong [34]. The need to discover novel marine actinobacterial is at its peak as the design for new and potent microbial bioactive agents is on the increase. Some of the discoveries which is on a geometrical increase are directed at biological applications of bio-polymers from the organism as antibiotics, anticancer compounds, single cell protein (SCP), enzymes and enzyme inhibitors, environmental recycling and cleaning agents, melanin's and probiotics in fishery and animal husbandry. From the forgoing, it is clear that scientific advancement today would in the near future create greater demands for the synthesis of novel bioactive compounds from marine actinobacteria [35]. Over the years, more than 97 new species of the marine actinobacteria have been reported by various investigators which represents 9 novel genera and 27 families of marine. Most of the studies have reported actinobacterial members from the Nocardioidaceae, Pseudo-nocardiaceae, Micromonosporaceae, and Demequinaceae families. The observation of new and multiple families of the actinobacteria has also resulted in the report of over 167 diverse bio-molecules and bio-active compounds from more than 56 species of actinobacteria and 24 genera. These observed bio-molecules from marine action-bacteriology have been applied for antimalarial treatment, environmental cleaning, antifungal, waste management, antibacterial, antiparasitic, etc. [36,37]. Most of these bioactive molecules are reported amongst Nocardiopsis species, Micromonospora species, Salinispora species, Brevibacterium species, Rhodococcus species, Arthrobacter species, Mycobacterium species, Pseudo-nocardia species, Kocuria species, with members of the Micromonospora species producing more bio-diverse bio-molecles [38,39]. In addition, other members of bacteria that thrive in the marine environment have also been found to be prolific producers of diverse bio-molecules including Microbacterium and Corynebacterium. Other actinomycetes representatives are found to be active and prolific producers of biological polymers/metabolites. The Streptomycetes group is economically the most important amongst the actinobacteria due to their relevance as potential and prolific producers of bio-polymers, producers of more than 10,000 identified antibiotics and high retrieval capacity (50%–55% is isolated) of the genus. It was reported that when searching for new bio-molecules within the marine ecosystem, researchers tend to overlook their role since their isolation strategies are specialized [35,40,41].

The Streptomycetes members possess specialized features, where most of such features are attributed to marine strains both for pharmaceutical, biotechnological and medical industry relevance as dated to their origin. A good number of such bio-molecules have been isolated, grouped into specific components and developed into drugs for the treatment of diseases in human, veterinary, and agricultural sectors [39,40,42].

It is also well established genetically that actinobacteria strains have a probable potential to produce 10–20 secondary metabolites as well as biological compounds, which has been applied for the production of over 75% of all known antibiotic and biotechnological products today. This feature is attributed to the biosynthetic gene cluster (BGC) of the actinobacteria members as revealed from the study of

Zotchevand his colleagues [43]. Streptomyces are the prominent source organism used in the production of many agents of therapeutic relevance including antibacterial (tetracyclines), antifungal (amphotericin), anticancer drugs in the form of Adriamycin and tacrolimus used as an immunosuppressant [39,43]. Hence, isolation, screening for biopolymer and characterization of species-specific strains of actinobacteria with potential for production of biomolecular agents as well as other therapeutics have been and will remain the most addressed part of ongoing research [44].

## 3.3. Approach to the exploration of marine actinomycetes

Following the observed potentials of marine actinobacteria and their biopolymer/bio-molecules especially for the removal and destruction/detoxification of pollutants, cleaning of industrial wastewater, detoxification of agricultural wastewateretc, various investigators have initiated interest in the exploration of these bacterial members.

The marine actinobacteria members have been shown to thrive/adapt well to an extreme environmental condition [45] and diversity of forms, physiology, morphology, genomics as well as possession of multiple metabolic capabilities [46]. Based on the diversity of potential possessed by the marine actinomycetes, specialized approaches are required to explore, isolate and/or characterize and harness their potential. Various conventional methods have been applied in their media isolation [47,48], in addition to diverse high-throughput molecular biology techniques, metagenomics, in insilico docking of biomolecules, culture-based approaches, etc. Recently, increasing knowledge on the functional character of actinobacteria has been observed, which is based on culture-independent and culture-dependent approaches with a view to obtaining viable but non-culturable (VNC) strains in addition to the one strain many compounds (OSMAC) phenomenon [38,49,50]. Below are some of the employed approaches to exploring these environmental restoring/remedial strains of microorganisms.

### 3.3.1. Fermento-cultural approach

Cultivation and growth on culture media of the marine-associated microorganisms has been an age standard employed for the exploration of diverse bacteria as it ensures investigators' observation of microbial cultural identity as well as morphological features of the bacterium. Whereas fermentation employs the survival abilities of an organism to break down multiple carbon sources by harnessing the metabolic proficiencies of members or strains of bacteria. According to Okudoh and Wallis [37], modern methods for the isolation as well as the fermentation of actinobacterial strains must employ a specific choice of substrate that encourages the growth of organisms; known cultural ingredients in media; specific incubation conditions and preliminary treatment; selection and optimization of organism type and method of purification [37]. Source tracking or targeting any actinobacteria member in the marine milieu would require astute knowledge of microbial characterization as well as experience in the area of such microbial taxonomy, environmental growth conditions (pH, cultivation temperature, oxygen, nutrient requirements) and physiology of the bacterium. The extreme conditions in the marine environment would have over time influenced and/or elicited specific features in marine organisms making these organisms acquire survival features in high salt concentrations (Salinispora species), in addition to utilizing diverse carbon sources including chitin, dextrose, starch, maltose, trehalose, glucose, mannitol, fructose, raffinose, fucose, glycerol and oatmeal [38]. These marine-associated organisms also have an existing interrelationship with their environments which makes it possible for their acquisition of diverse explorable potentials. With the aforementioned in mind, specific and special culture media are designed to grow the marine organisms and evaluate their proficiency as prolific sources for the production of specific bio-molecules. Hence, major actinobacteria culture media employed during exploration studies must possess low nutrient and be supplemented with some nutritional components, as well as the inclusion of marine water, marine sediments, sponge extracts, transition and trace elements, and other additives suggested by numerous investigators. During isolation of organisms, diverse media and numerous strategies have been employed to successfully isolate the marine-associated actinomycete members. These include multiple isolation media; the media must contain a specific choice of substrates at a required amount for the actinobacteria of interest; the need for growth-limiting materials to prevent growth of unwanted organisms; addition of chemicals and antibiotics as growth inhibitors for bacteria, fastidious organisms, and fungi; and media must mimic natural environments and conditions to encourage growth [39,50–54].

Recently, culture-dependent and independent reports describe the existence of ocean/marine derived indigenous marine actinomycetes, which produce active bio-molecular components of both environmental and clinical relevance [55–57]. These members are, *Rhodococcus sp.* [58], *Streptomyces sp.* [56], the newly described genera *Salinisporasp* [59–61] and *Marinispora sp.* [59,62] which are hydrophils.The*Aeromicrobiummarinum* reported by Bruns et al. [29] is salinophilic. A genus which can only tolerate 10% NaCl and not salinophilic is Salinibacterium [63]. Another indigenous actinobacterium isolated in the marine is Verrucosispora strain AB-18-032 [64] and was found to produce salinosporamides, a potent anticancer agent now on clinical trials [65]. Fermento-cultural exploration actinobacteria strains which posses astute potential for the production of active bio-polymers remains one aggressive area of recent attention as the drive to resolve various concerns of man and environment continues to titivate. The characterisation of such numerous novel marine actinomycetes with metabolites of natural origin [66], and potent bioactive production potential in different habitat has also reveal stability with recognisable output and such studies are ongoing [39,59,67–71]. It is important to note that chitosan, although a natural biodegradable bio-polymer derived from chitin after a controlled deacetylation process, the fermento-culturally derived product possesses better heterogeneous features as regards its physiological and chemical potential [72–74]. In the cell wall of most fungus, chitosan has been reported to be involve in maintaining cellular structure, shape, integrity and strength hence when grown in a simple media, it can be easily extracted [75,76]. Such fermented derivatives of chitosan have shown better and great heterogeneity with broad usefulness spectra.

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#### 3.3.2. Post-cultural and non-cultural genomics

During the early discovery of the potentials of marine bacteria strains, major culture-dependent and independent studies of actinobacteria have been faced with both cultural confirmation of prolific organisms and the gene locus of interest. The concern also includes the nucleic acid type, gene region, gene type, gene sequence, functional proteins, protein sequences and other gene regions that interrelate with the specific gene region for the functional amino acid sequence of the gene. In recent times, bio-synthetic gene clusters (BGC) and the molecular structure of bio-polymers were also reported as important post-cultural genomic studies. The advent of DNA sequencing and the application of advanced molecular biology techniques in microbiological methods in the last forty years have revolutionized the field of science. Diverse concerns and questions associated with life in the marine habitat as well as the microbial studies and their economic relevance for human and environmental wellness have changed for the better with regular research outputs and innovations. DNA sequencing and molecular biology applications have enhanced tracking of genetic markers to the specific locus with historical traces of such gene-based indicators. It has also revealed and arouse interest in metagenomics while mapping the various microorganisms in diverse niches [78]. These specific areas of impact from DNA sequencing and molecular biology research have aroused a growing interest in conservation of life, which has also encouraged distribution of genealogical lineages and phylogenesis [79]. In addition, the mapping of species' genetic patterns and metagenomics (genomic analysis of microbial nucleic acid assemblages) of the marine niche microbes [80] is not left. According to Skoglund and his colleagues, the methods include random sampling of marine environments, DNA extraction from collected samples, polymerase chain reaction or amplification of nucleic acids and library preparation of extract and sequencing of nucleic acid [61]. However, when cultivation may be required, an additional enrichment of potent microorganisms may be another step before extraction of nucleic acids [61]. Although the aforementioned impacts have been derived/employed in affirming the whole genetic profile of marine-associated organisms and enable researchers to explore the microbial components, the cultural applications have never been relegated or disregarded. Cultural and preliminary determination of bio-polymers and bioactive molecules from the media of actinobacteria would remain relevant especially as the need to affirm the in vivo activity is part of ongoing studies.

### 3.3.3. Insilico-biomolecular targets

Obtaining the biological function of various active bio-polymers and molecules is another essential area when discussing the exploration of actinobacteria in the marine habitat. The necessity is indubitable as it will enhance the understanding of cellular response to targets and usage as part of components for structural-based design (SBD). A high throughput into genomic studies has yielded putative sequences that lack functional annotation [31], however, homologous modeling has been used to assign biological function to multiple unknown bio-molecules. This is true, as more than 50% similarity in sequences of genes implies corresponding similarity in the gene functions and structure. Homologous modeling provides functional assignment for approximately 50% of proteins identified in various proteomics studies, while structural genomics is augmenting the functional assignment of various hypothetical proteins by determining the corresponding three-dimensional structures. Insilico-based studies of bio-molecular components may be a post-sequencing experiment that involves sequence homology studies which ensure an appropriate assigning of function to a specific gene sequence from an organism. It would also define the possible activities of the bio-polymer or bio-molecule in any given environment and at a specified reaction media [81,82]. During in insilico-based design of bio-polymers or other bio-molecules the target of the polymer as well as the possible reactions would also be ascertained. Researchers would also be able to identify components that may serve as ligands, act in combination with a polymer and any presumed in vivo action especially for those that may be used for in vivo activities (**Figure 1**).

One emerging and novel area of biotechnology is the science and technology that applies microorganisms from the marine habitat, their products and other support agents for improved livelihood. The understanding of genomic concepts in the marine and possible applications would be useful in bioenergy development and other spheres of human existence.

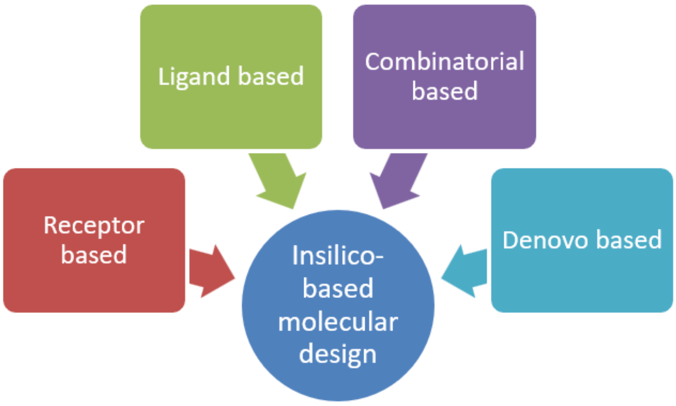


**Figure 1.** Approaches ofinsilico-based biomolecular design.

### 3.4. Chitosan and its derivatives in nanotechnology

With a view to advancing research and technology, recent reports have been focused on chitosan which is a natural biodegradable polysaccharide produced from chitin by the deacetylation process [83,84]. Due to the relevance of the bio-polymer in various scientific disciplines, attention has been given to its source and its usability resulting in research-driven interests. Interestingly, the bio-polymer has been applied in drug and antibiotic production against numerous bacteria, fungi, yeast, etc. [2,85–89] because of its antimicrobial potency and activity. The molecule has also been applied in other areas of biotechnology and nanotechnology, which various recent investigators have termed nanotechnology. In such regards, the chitosan and its derivatives are prepared by the introduction or addition of hydrophobic groups, fibers of banana, capsular coatings, metallic coating, glass coatings, etc., by cross-linking agents such as glutaraldehyde. The prepared component which may be in the form of a nano-sized reinforced composite is called nanochitosan. The product may also be characterized using state-of-the-art analytical tools including TGA, DSC, XRD, FT-IR for nanosized thermal stability, types/class and effectiveness.

In the real world, it is expected that the features/properties, stability, chemical behavior, and nanomaterial types are regularly characterized and improved to meet global relevance which will in turnopen new and great opportunities for an emerging field of research. To parse with the growing science needs and the new era of 'green synthesis' approaches/methods, it is expedient to understand the interest of current research and development on materials, science and technology. Basically, one must understand how the green synthesis approach for materials of relevance and/or nanomaterials works, how it is produced via controlled regulation, how it can be applied in cleanup exercises and remediation processes. An adroit look at the aforementioned would help uplift its usefulness and its environmental friendliness. It would also revolutionize waste control, prevention, minimization of waste, reduction of pollution, and the application of safer (or non-toxic) solvents/auxiliaries and build-up of a reliable, sustainable, and eco-friendly environment.

### 3.5. Diverse application of nanochitosan

Nanochitosan as a biological architectural material has been applied in multiple disciplines due to its unique non-toxicity, biodegradability, biocompatibility and antimicrobial activity. Other features include stiffness, strength and heat resistance which enhance its use in mobile delivery of immunogenic agents, subunit vaccine production as well as adjuvants, cellular purification of biomolecules, food industries as additives/storage agent, thin film bio-immobilization of agents, probing of DNA, bio-label fluorescent technique, biosensor development nano-fertilizers, etc. [17,18,90–92]. The application of nanotechnology in addition to the diversity of properties possessed by chitosan, has been used in agriculture to prevent nutrient loss or leaching, resulting in agricultural sustainability. This new scientific discipline, which utilizes semi-solid and solid synthetic materials for environmental remediation, waste reduction and/or pollution control, in situ delivery of bio-molecules ecotoxicological sustainability and renewal of energy, clinical diagnostics, pharmaceutical and biotechnology is currently receiving attention in various global sectors. The biocompatible feature of chitosan has ensured its usability for both hard and soft material applications in science, agriculture and medicine. Suffice it to say that nanoparticles are small or minute particles of one-dimensional crystal or powder of about 1 nanometer = $10^{-9}$ m or 1 billionth of a meter [93]. Based on this study, three major areas, which include animal husbandry, aquaculture and food conservation were discussed.

### 3.6. Animal husbandry

Animal husbandry is another area of agricultural science that involves the breeding, feeding, tending and management of domestic animals. This area of science has received attention in recent times especially amongst farm animals due to interest in sustainable agricultural development and making food available for all. Following the study of Albulov and his colleagues, it was reported that the management of farm animals, the administration of vaccines to avoid infection and improve farm yield are key steps that are regularly employed [20] during the agricultural process. With the interest of improving animal production and enhancing the process of animal husbandry, various investigators have reported the use of chitosan-succinate as an adjuvant, which is added to vaccine subjects in the control of animal necro-bacteriosis. Suffice it to say that diverse microbial activities such as resistance [94–98] have resulted in the distribution of diseases and poor agricultural products. This approach has provided the required vaccine immunogenicity with a simultaneous high value on the hemagglutination test. In addition, chitosan has also been applied in animal husbandry or farming to serve the purpose of a drug delivery system for antibiotics, anesthetics, and painkillers; as an ingredient in domestic animal feeds; for milk production; as a growth-promoting factor for mucosal epithelium, antiparasitic and immunomodulatory agent for mucosal associated lymphoid tissue [41,99–104]. Another area where nanochitosan has been reported relevant is blood anticlotting and hemostatic effect in the form of microsphere. The application of chitosan-based components or molecules in wound dressing has shown dependability in controlling arterial hemorrhage among dogs [105]. In addition, chitosan based molecules have been used as anti-thrombogenic and anti-coagulating agents, e.g., N-hexanoyl, lipoprotein lipase (LPL), Chitin 3,6-sulfate and

N-octanoyl-chitosan fibers which are employed as anti-thrombogenic and anti-coagulating agents [92,106]. Others are used as phthalates with chitosan derivatives for anti-thrombogenic molecules applied during vascular grafting [107,108]. One notable future of nano-particulate bio-molecules is their usefulness as the best biomedical material due to their biocompatibility, high covalent bonding, properties and bioactivity making the relevance of nano-type bio-molecules of great relevance in animal husbandry as well as improved yield of animals.

### 3.7. Aquaculture and aquaponics

In recent times there has been a drive towards agro-improvement and a need to make food available to all, which has propelled the area of aquaculture and aquaponics. These are an area of agricultural advancement that operates a system that favors increasing economic and sustainable indoor and outdoor fish farming with improved efficiency both in farm health and productivity. Chitosan, its derivatives and the advanced technology (nanochitosan) are made in combination with aquaponics (aquaculture with hydroponics) to obtain a novel study area called aquaponic-chitosan [109,110]. This new area employs the principles of sustainable agriculture (wastewater bio-filtration for plant use to produce the nutrient-rich food and increased yield of fish farm product) [85]. According to some investigators, chitosan is added as a dietary supplement for fish farms, biofilters, bio-fertilizers, bio-pesticides, enhances physiological plant response to abiotic stress, while mitigating its adverse effect via the stress transduction pathway. It also stimulates photosynthetic activities and energy metabolism during stress [21,111].

### 3.8. Food conservation

In food conservation which focuses on the management and control of changes in food physicochemical properties, chitosan is used to introduce hydrophobic groups and coating capsules which aid in enhancing the food's physiologic features. The application of nanochitosan based particles may also enhance the physicochemical modification of food and also improve the bioavailability of functional food [112]. In a similar study, Nguyen and Nguyen, also observed an improvement in the effects of nano-particulate-based chitosan and chitosan-coating on strawberries' physicochemical properties, which are kept under storage [90]. Their findings revealed that coating strawberries with 0.2% or 0.4% nano-chitosan possesses a tendency to preserve the total quality index of strawberry fruits for as long as 21 days. Other secondary effects include reduction of weight loss, increased titratable acidity with high L-ascorbic acid, retained firmness of fruits, inhibited polyphenol oxidase activity and a significant reduction in malondialdehyde production amongst fruits during storage [90]. Another aspect was chitosan and its nano-type derivatives are employed in electrospun fibers used for wrapping dry-aging materials. It has shown up upto three weeks of storage of dry-aged beef and preservation from microbial proliferation. Other related studies have also reported the use of synthetic nano-type chitosan and biopolymers to conventionally cover edible food, which provides resistance to microbial proliferation and moisture resistance [30].

### 3.9. Problems of exploitation of nanochitosan

Although nanochitosan possesses astute potential and usefulness in diverse real-world applications, several problems have been associated with its usage. In food packaging and conservation of food, there is an impossibility of continuous application of nano-type chitosan which is associated with water vapor content of material, weak mechanical resistance and weak sewing [113]. Chitosan and its derivatives individually have shown poor relative deterioration capacity against water vapor; hence, to improve on these demerits, they are incorporated into high moisture-resistant components [30,114,115] to compensate for chitosan's high hydrophobicity. According to most investigators of related studies, this concern may be overcome by decreasing the hydrophobicity of synthesized bio-polymers via pretreatment [74,116–120]. Although the application of the aforementioned has enhanced scientific drop ties, this strategy has been reported to result in the loss of polymer bioactive potency, the need for intricate tools for application and cost effectiveness [121]. Another strategy for reducing hydrophobicity is by making the biopolymer super-hydrophobic [53]. These alternatives have been reported/applied both in studies and experiments by various investigators [53,113,122].

### 3.10. Global knowledge gab in marine derived nanochitosan

Globally, there has been a research interest, knowledge-scape, research reports, applications and alternatives in various real-life processes on the usefulness/capabilities of chitosan, its derivatives and the nano-type molecules. However, this multifaceted knowledge has shown poor research-based documentation, as well as progress in terms of biotechnological applications. The study of Cheung and his colleagues revealed the Scopus-indexed publications of related studies from 1985 to 2015 with a relative annual publication growth [110]. However, assessing the various applications from published documents to real life has been a concern. Although such an increase in publications has revealed globally known capabilities as well as research-based knowledge and/or application of the nanobased chitosan particle, there has been poor documentation and application of the progress made thus far. An open accessibility to industrial applications of such progress in chitosan knowledge-research-based documentation has a part in global future research. It is also a suggestive way forward for documentation of biotechnological advancement/application of nanochitosan.

### 3.11. Marine actinomycetes derived nanochitosan

The marine niche has been seen as one of the most important extreme environments on the globe due to the uniqueness of life and the diversity in forms of life. It is characterized by bacteria with distinct features and important source of bioactive bio-polymer. The marine environment has been documented to consist of 16 trenches with a depth of 7000 m (www.submarine_topographical_features#List_of_oceanic_trenches) in the world [49]. The marine and deep-sea oceans are also the most extreme environments with the richest record of biodiversity which surpasses that of the coral reef and rain forest. Microorganisms in these habitats possess the capacity for extreme biochemical and physiological activities [123]. Some members of the culturable actinomycetes that are associated with the marine habitat are *Kocuria specie, Rhodococcus specie, Microbacterium specie, Streptomyces specie, Arthrobacter specie, Brevibacterium specie, Micrococcus species, Nocardiopsis species, Pseudonocardia specie, Mycobacterium species, Corynebacterium species,* and *Actinomyces species*. These members have been reported to produce a medium chitosan molecule following a cultivation and fermentation process in a specialized media component. The nano-type chitosan derived from its product has been reported with versatile biological relevance to scientific studies and biotechnology.

### 3.12. Future prospects and relevance of marine derived nanochitosan

Chitosan is a biodegradable and low-cost biopolymer that in recent times has been sourced from marine microorganisms especially the actinobacterial members. Its numerous capabilities and applications in pharmaceutical industries, biotechnological industries and medicine have welcomed diversity of interest. Technological advancement has also enhanced its usage as a nano-particle for drug delivery, diagnostics, and research advancement. Marine-derived chitosan and its nano-type bio-molecules have been widely studied and knowledge on their relevance and potential in diverse environments/disciplines is still increasing. Because of their nontoxic nature, ease in diffusion, biodegradability, metabolic proficiency, absorption, adsorbent, stabilization, etc., it is possible for them (chitosan and its nano-type derivatives) to be engineered into scaffolds and molded into diverse anatomical shapes to provide short-term mechanical support for biological materials. The biocompatible nature of the bio-polymer is an all-encompassing feature that can be harnessed into biological processes involving plants, animals and man. It is hoped that in the future, as its knowledge-scape continues to increase, the bio-polymer will be bio-engineering into biological materials to enhance bio-pollution control, bio-remediation of waste or bio-recycling of various categories of waste. This would enhance environmental wellness, cleanliness and public health since there would be bio-controlled degradation of environmental waste. The impact would also be received in agricultural advancement as there would be prompt delivery of required nutrients for plant improvement to farmlands (nanochitosan-based fertilizers). The advancement of the technology of chitosan may also buffer the recent application of the Internet of Things (IOTs) in mechanized agro-ventures and prevent the tendency for the spread of infection or diseases amongst farm crops/fruits. It would also result in improvement in animal husbandry as well as treatment/control of livestock diseases. It is also hoped that the biomolecular versatility, biocompatibility, polycationic and nontoxic nature of nanochitosan and its derivatives may be used as nano-type quaternized chitosan (QNC) with activity that depends on charged molecules and targets that may be directed at positively charged quaternary groups, nucleic acids (DNA and RNA), proteins and amino acids, hydroxyl and carboxylic ions.

## 4. Conclusion

It is not gainsaying that one noteworthy novel and emerging area of biotechnological studies has remained the application of microorganisms and their improved strains from the marine habitat (Actinomycetes). The diversity of its biochemical products and other supporting agents for improvement of livelihood for men, animals and plants has shown relevance with welcomed interest in diverse sectors. Such growing scientific strides have been harnessed principally by the understanding of genomics (metagenomics), proteomics and culturonomics in recent times, which has also enhanced scientific studies especially among biopolymers sourced from marine niches. Following the aforementioned relevance of non-based chitosan as well as the potential relevance of the bio-polymer in various sectors of science, health and engineering, an ongoing interest has been aroused if it is strategically harnessed. Such ongoing interest extends to revamping the aquaponic and aquaculture sector that may also be experimentally useful by the application of nano-type chitosan derivative which promises to enhance water-associated culture of life, including fish farming. It has also shown some notable therapeutic relevance from the studies of related investigators. As a potential therapeutic molecule, the polymer is a suggestive drug lead in the management of tumors since it has shown proficiency in the induction of cytokine production via proliferation of T-cell and inhibition of pro-apoptotic mechanism against tumorigenic cells. It may be applied in wound-care technology and improve the phage therapy technology of excruciating wound infections. As a highly adsorbent bio-polymer, it has shown increased environmental friendliness, inexpensiveness, versatility, biodegradability and selectivity, making it a potential stain/dye remover and metallic pollutant or organic waste remover. It is hoped that, based on its versatility and biocompatibility, the bio-polymer may be used as a nano-type quaternized chitosan with activity that depends on charged molecules and targets may be directed at positively charged quaternary groups, nucleic acids (DNA and RNA), proteins and amino acids, hydroxyl and carboxylic ions. Such advancement would give birth to a new approach to scientific research, improve molecular studies, biotechnological processes, pharmaceutical companies, and diagnostics/medicine, and revolutionize industrialization.

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