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Review article

Exopolysaccharides from bacteria and fungi: current status and perspectives in Africa

Osarenkhoe Omorefosa Osemwegie [a,*], Charles Oluwaseun Adetunji [b], Eugene Ayodele Ayeni [a], Oluwaniyi Isaiah Adejobi [a,c], Rotimi Olusunya Arise [c], Charles Obiora Nwonuma [d], Abbot Okotie Oghenekaro [e,f]

[a] Department of Biological Sciences, Microbiology Unit, Landmark University, P.M.B 1001, Omu-Aran, Kwara State, Nigeria
[b] Applied Microbiology, Biotechnology and Nanotechnology Laboratory, Department of Microbiology, Edo University Iyamho, PMB 04, Auchi, Edo State, Nigeria
[c] Chinese Academy of Sciences, Kunming Institute of Botany, Key Laboratory for Economic Plants and Biotechnology, Yunnan Province, China
[d] Department of Biochemistry, University of Ilorin, Ilorin, Kwara State, Nigeria
[e] Department of Plant Biology and Biotechnology, Faculty of Life Sciences, University of Benin, PMB1154, Benin City, Edo State, Nigeria
[f] Department of Plant Science, University of Manitoba, Winnipeg, MB R3N 2N2, Canada

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ABSTRACT

Bacterial and fungal exopolysaccharides (EPSs) are extracellular metabolites of living organisms (plants, animals, algae, bacteria and fungi) associated with adaptation, survival and functionalities. The EPSs also afford humans multiple value-adding applications across different spheres of endeavors. The variable chemical and biochemical architecture that characterizes an EPS presets its biological functionality and potential biotechnological benefits. Suffices to say that it is amenable to genetic, biotechnological and biochemical maneuverability for desired bioactivity or application during their production and extraction. EPSs have been shown to have, antioxidant, anti-tumor and antiviral activities; enhance soil aridity and nutritional value of food consumed by humans. Their innocuous domestic and commercial versatility and biotechnological relevance is a reliable confirmation of the recent attention accorded EPSs by the global research community. This is especially with respect to their biosynthesis, composition, production, structure, characterization, sources, functional properties and applications. It is also responsible for the development of newer strategies for their extraction. EPSs' relative prospects, perspectives and orientation in the African context are seldom reported in recognized scientific literature data bases. A random preliminary study showed that EPS applications, biotechnological and research orientations are still developing, and influenced by preponderant vegetation, level of industrialization, political will and culture. Africa is endowed with untapped bioresources (biomaterials), bioproducts and bioequivalents that can mediate several global foods, industrial and technological challenges for which EPS may be a potential remedy.

1. Introduction

Biopolysaccharides, a group of biopolymers are generally consistent with structural (membranes and walls) and the compositional (cytosolic polysaccharides) integrity of living things [1]. They are biodegradable, biologically and biochemically variable, and compatible with the environment, biomes and humans. Additionally, they are known to be produced by stress-stimulation in bacteria, algae, fungi, animals and plants [2]. The world witnessed, towards the last decade, an improved consciousness of the inherent utility potentials of biopolysaccaharides derivable from different biogenetic resources. This unique attraction to biopolysaccharides is resulting in the emergence of variably bioactive, inexpensive biosulfactants, bioemulsifiers and exopolysaccharides of diverse biotechnological, pharmacological, industrial and medical applications [3, 4, 5]. The imperative need by humans for safer natural remedies that are environmentally and biologically friendly compared to chemically synthetic polymers is responsible for the paradigm shift to biopolysaccharides exploration. Furthermore, the rising multifunctionality profile of biopolysaccharides as reported by Polak-Berecka *et al.* [6] also affirmed the continual and global attraction to biopolymers. Chemically, they are complex biomolecules (macromolecules) composed of not less than 20 monomeric sugars (glucose, fructose, rhamnose,

* Corresponding author.
E-mail address: osemwegie.omorefosa@lmu.edu.ng (O.O. Osemwegie).

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galactose, N-acetylglucosamine, glucuronate, N-acetylgalactosamine) linked together by glycosidic bonds formed by a reaction between hemiacetal hydroxyl group of one monomer unit with the hydroxyl group of another [7]. Biopolysaccharides could be characterized as either a *homo-* or a *hetero*-polysaccharide with branched or unbranched monomeric configuration that affords rheological, physicochemical and novel bioactive functionalities [8, 9, 10]. Homopolysaccharides include Cellulose (D-glucose residues joined by β (1→4) glycosidic bonds), and Chitin (N-acetyl-D-glucosamine joined by β (1→4) glycosidic bonds). On the other hand, heteropolysaccharides include hyaluronan, which is composed of 250 to 25,000 β (1→4)-linked D-glucuronic acid and β (1→3)-linked N-acetyl-D-glucosamine. Chondroitin-4-sulfate, another heteropolysaccharide consist of D-glucuronic acid and N-acetyl-D-galactosamine-4-sulfate. Unlike biological proteins which are genetically encoded and well studied, the specific or designated size of many biopolysaccharides remains unclear.

The formula of polysaccharides is $C_x (H_2O)_y$ where x is the number of carbon backbones. They may also be categorized as natural or synthetic compounds based on their origin [11]. Biopolysaccharides are integral to the architecture of living things and a wide variety of them are produced by bacteria and fungi. A wide variety of these occur in their structural, intracellular, and extracellular (exocellular) integrities to primarily facilitate adaptability, communication, eco-physiological resilience and mechanistic survival in diverse natural habitats [12]. The present status of higher plants and marine algae as the largest sources of biopolymers is becoming paradoxical since the discovery of bioequivalent alternative biologically active EPSs in bacteria and fungi. Bacteria and fungi were reported by Donot *et al.* [2] and Ates [4] to be fast and high yielding biopolymers sources without complicated extraction technology requirement [2, 13]. This is in addition to their being readily available, versatile and valuable biogenetic resources. A shift from plants and algae as sources of biopolysaccharides for human biopolymer needs may be due to the growing demand pressure for biopolymers either in the form of biotechnology or research raw materials or products which afford multiple utilities. Consequently, this has pushed up the global market price values of biopolymers. Furthermore, scientific debates alluded to the fact that over-dependence on aquatic and terrestrial greens of the earth for economic, energy, technological, food, pharmacological and medical needs of humanity is directly responsible for the challenges of global warming and climate change [8]. These factors mentioned above rightly justifies the shift by polymer researchers to non-producer sources, energy-efficient, renewable, non-toxic sources that do not require arable lands for cultivation or depletion of photosynthetic producers as alternatives [14, 15].

Exocellular polysaccharides (exopolysaccharides-EPSs) are regularly excreted from the membrane level into the environment making them apparently unattached, renewable, free and easily extractable from orgasmic biomasses by specialized fermentation techniques [16, 17]. The underlying mechanism of microbial polysaccharides synthesis and translocation remains rudimentary and hypothetical. According to Schmid *et al.* [18], chemical condensation of intracellular nucleotide sugars and other starter precursors in a combination of metabolic pathways may be responsible for their synthesis. The mechanism of EPSs production is predisposed to influence by the environment and physical factors [6, 14].

Bacteria and fungi EPSs are long-chain polysaccharides synthesized throughout their ecological existence. They are composed of branched and repeating units of sugars connected by 1, 4-β- or 1, 3-β-linkage in strongly rigid polymers or 1, 2-α or 1,6-α linkage in flexible polymers [19]. They are high molecular weight compounds with distinct physiological and ecological roles that include communication (signal-receptor) dynamics, defense against predation, hydration and detoxification of chemicals, movement, adhesion/attachment to surfaces, pathogenicity, interaction with proteins and selective sequestration of metabolic prerequisites [20, 21]. EPSs also witnessed wide biotechnological applications as an emulsifier, product stabilizer, immune-modulator, therapeutics, thickener and flavoring agents, drugs, and food [22]. According to Gonzalez *et al.* [23], extracellular biopolymers expressed from both bacteria and fungi compete favorably with those from plants and algae sources in chemical quality, bioactivity, relevance and effectiveness. These EPSs differ from those of plants and algae in purity, finiteness, and are more environmentally friendly. They afford a simple isolation process that is inexpensive, sustainable, high yielding, non-toxic, more rheological and pseudoplastic. A diverse range of natural polysaccharides occur in living organisms such as bacteria, fungi, plants, algae, and animals. In recent decades, synthetic or semi-synthetic polysaccharides have been produced by chemical or enzymatic alteration of macromolecules which have found access to the biopolymer markets [11]. Their role in the synthesis of nanoparticles (particles of the size range 1–100nm) and biogas production has been documented [24, 25, 26]. Exopolysaccharides are reported to express several biological activities that may include antibiotic, antioxidant, anti-mutant, anticoagulant, and immuno-stimulant properties [27]. These polymers also have important taxonomic values, ecological implications in the storage of energy, and usefulness as biomarker of environmental change or stress [13]. Consequently, they are now attractive as renewable biotechnological and protein engineering resources that could be appropriately exploited, modulated and obviously transformed into several value-added products for human benefits [11].

The slow utility of exopolysaccharides in Africa is facilitated by their observed scarcity in value addition to humanity. While the reason for this could not yet be scientific ascertained, logic may link it to the state of knowledge and technology growth in the continent. This inadvertently supports the growing perception on the inadequate state of published works on exopolysaccharides from African traditional, industrial, environmental and healthcare backgrounds. The compromising effect of humans' constant dependence on the diverse aquatic and terrestrial vegetations within the global space on ecosystem health, functions and resilience is also of growing concern as well as a motivator for the present review. Recent emerging challenges from global climate perturbation coupled with emergent environmental and health repercussions from human persistent reliance on various brands of synthetic chemicals, drugs, agro-allied and non-biodegradable plastics has railroaded the scientific communities to seeking possible safer, organic, bioequivalent alternatives with matching bioactivities. Consequently, alternative richer sources of naturally occurring non-vegetational biotechnologically valuable resources are becoming apt as direct raw materials or products' agents of human benefits. Therefore, this review gives an overview of the potential values of exopolysaccharides from bacteria and fungi. It focuses on the African continent and attempt to provide analytical information from Scopus, Scihub and PubMed platforms on the current position of African scientists' contributions to the recent advances recorded on the full applications, isolation, and biotechnology of bacterial and fungal exopolysaccharides. This compressive compilation is intended to facilitate knowledge, research and screening of Africa's bioresources for microbial EPSs and serves as the basic reference on African EPSs.

2. Mechanisms of exopolysaccharides biosynthesis

There is a slow empirical progress made in providing clarity on the biosynthetic mechanisms and biochemical pathways, leading to the production of bacterial and fungal exopolysaccharides. The versatility of EPSs is apparently mediated by the understanding of the underlying precursors required for their biosynthesis or mechanisms which may be growth-phase dependent [4, 28]. The biosynthesis of homopolysaccharidesis is theoretically different from that of heteropolysaccharides [29]. Bacterial heteropolysaccharides are mostly generated intracellularly and transported to the extracellular environment whereas homopolysaccharides are produced externally to the cell by an enzyme secreted by the bacterium. The enzymes involved in EPS synthesis are located at different cellular regions and can be categorized into four groups based on their involvement in the last three of the four

steps of bacterial EPSs syntheses [30]. Similarly, Madhuri and Prabhakar [31] posited that biochemical syntheses of exopolysaccharides are complicated by the involvement of encoded genes for enzymes and precursors that serve as intermediates in protein regulation and central carbon metabolism.

The first group includes intracellular enzymes such as hexokinase which phosphorylates glucose (Glc) to glucose-6-phosphate (Glc-6-P), a possible intermediate metabolite for the formation of sugar nucleotides (UDP-glucose and dTDP-glucose). This also functions in other cellular metabolisms. The second group stage of synthesis is the catalysis of sugar nucleotides. Uridine-5′-diphosphate (UDP)-glucose pyrophosphorylase converts Glc-1-P to UDP-Glc, one of the vital molecules in EPS biosynthesis. The third group stage includes the action of glycosyltransferases (GTFs) which are localized in the periplasm. GTFs transfer the sugar nucleotides to a repeating unit linked to glycosyl carrier lipid, identified as isoprenoid alcohol [32, 33]. The polysaccharides are then modified through such enzymatic activities as acylation, acetylation, sulphation, and methylation, and exported to the extracellular surface with the help of hydrophobic enzymes like flippase, permease, or ABC transporters in the fourth stage of the synthesis [33]. It could be assumed that the functional purpose of the EPSs induced by ecological factors is encoded at the enzymological stage four of the biosynthetic process to create the versatility associated with exopolysaccharides.

Schmid *et al.* [18] and Hong *et al.* [34] posited other hypothetical mechanisms for exopolysaccharides biosynthesis. These mechanisms are enumerated as follows:

(i) Wzx/Wzy dependent pathway for O-antigen synthesis by bacteria may offer the best possible explanation for EPSs systematic production. This involved the binding of activated sugar with lipid carrier (undecaprenyl pyrophosphate) via glycosyltransferases (GTFs) action to form a defined sequence of repeating units for transport by Wzx protein (flippase). Polymerization occurs at the periplasmic space catalyzed by the Wzy protein before they are exported to the cell surface [4, 35]. Ates [4] reported that EPS biosynthesis occurs via the Wzx/Wz-independent and Wzx/Wzy-dependent pathway.

(ii) The ATP-binding cassette (ABC) transporter-dependent pathway involves periplasmic proteins, the PCP and OPX family [36]. Like the Wzx/Wzy dependent pathway, the ABC transporter-dependent partway also uses GTFs in polysaccharides formation before their export from the cytoplasm through the tripartite efflux pump complex. The possible involvement of ATP-binding and depolymerization (hydrolysis) actions at the nucleotide-binding domain (NBD) exerted conformational changes on the membrane heterooligomeric complex of the outer membrane polysaccharide export (OPX) protein and polysaccharide copolymerase (PCP). This synthetic dynamic may possibly be the reason for the observed functionalities and chemical architectural (form) divergence of exopolysaccharides. Consequently, the ABC transport-dependent pathway is assumed to be a more appropriate biochemical description for the formation and excretion of capsular polysaccharides of microorganisms than the previous mechanisms mentioned on EPS synthesis. Further insight into the dynamic of this pathway is provided in the review paper by Liston *et al.* [37].

(iii) The synthase-dependent pathway has the advantage of exporting EPSs with or without the benefits of lipid acceptor molecules. Also, polymerization of EPS precursors and eventual transport of the molecule are facilitated simultaneously by a single synthase protein and a membrane-localized GTF [38]. Complete polymer strands of repeating units are transported across the cell membrane by flippase suggesting a more peripheral location for the EPS synthesis. Furthermore, synthase-dependent pathway compared to others is independent of the central carbon metabolism. It is uncomplicated and may only afford the production of EPSs with limited functional versatility and chemical architecture [39].

In (i) – (iii) above, activated sugars/sugar acids are enzymatically generated inside the cell. The extracellular synthetic pathway alternatively elongates the polymer strand by direct addition of monosaccharides obtained from the cleavage of di- or trisaccharides complexes [35]. The knowledge of EPS gene organization affords a basic understanding of the systematic stages (chain-length determination, polymerization, and export) in its production mechanism without comprehensive suggestions on the physiological, metabolic and environmental parameters regulating and stimulating EPS biosynthesis. Numerous studies have demonstrated the influence of biochemical structure on phenotypic functions. The architecture of the EPS molecules affects their solubility, polarity, electrolyte activity and metabolism. The size of the molecule, its branching rate, and form have also been reported to influence their biological activity as exemplified by the β-(1→3) bonds in the main chain and β-(1→6) branches which strengthened the fungal glucan structure and conferred on it an anti-tumor property. It is reported that β-(1→6) linkages alone would confer lesser activity [40]. As a result, most enzymes that are active against EPS have to be isolated from three main sources: endogenously from the EPS-synthesising microorganism, exogenously from a variety of other microorganisms or bacteriophage particles [41, 42]. Several approaches are employed in degrading EPSs, the majority of which are based on a mixed-enzyme system that combines a variety of activities. For example, galactosidase, galacturonidase, rhamnosidase, fucosidase and α-glucosidase mixture have been used to treat microbial slime in industrial water systems [43], and a combination of β-glucanase, α-amylase and protease also used for removing slime [44]. However, these approaches have not been sufficiently well developed to constitute a full-scale alternative to chemical biocides [45].

3. Production method of bacteria and fungi polysaccharides

The prefix *exo*-suggests that the compound occurred in the outermost part of both bacteria and fungi where they tightly interact with the cell structure or are excreted in other limitless ecophysiologically functional forms e.g. protective shield, signals, ligand, enzymes or allelochemicals. Excreted biopolymers occur as loose fitting cell-environment interface that is comparatively easier to isolate and purify. The range of methods reported in scientific literatures was preferred based on their non-drastic approach that preserves the physicochemical properties and functionalities (structural, sorptive, surface-active, nutritive, informative and redox-active) of the product [20, 33]. Consequently, a combination of physical (e.g. colorimetry, sonication, centrifugation, heating, freeze-thawing, microwave treatment), chemical (e.g. cationic exchange resin, glutaraldehyde, alkaline, NaOH, ethylenediaminetetraacetic acid-EDTA, formaldehyde) and analytical (HPLC, GC-MS, FTIR, NMR) methods were adapted for isolating exopolysaccharides from bacteria and fungi, especially the food grade types [2, 46]. In nature, the architecture of exopolysaccharides is defined by repeating monomeric sugar moieties whose individual and combined chemical characteristics afford a diversity of reactive responses and functions. Some of these behaviors are evident in their association with other molecules including proteins (glycoproteins) and lipids (glycolipids). This may have been linked to the secretion of a variety of other metabolic by-products during isolation from the cell necessitating the need for purification by chromatography, electrophoresis or solvent extraction. Affinity, ion-exchange, size-exclusion, and thin-layer chromatographic techniques were reported by Nelson and Cox [47] to be suitable for the isolation of exopolysaccharides.

Different fermentation technologies are reported and adapted in controlled-environment for the production of bacteria and fungi exopolysaccharides, and other highly beneficial substances [4]. Fermentation exploits the metabolic activities of organisms for the bioconversion of complex substrates under anaerobic conditions. At the same time, the

organisms release new compounds called secondary metabolites, which may include exopolysaccharides. The standard products of fermentation include alcohol and carbon dioxide with polymerization monomers for the production of polysaccharides. Two major types of fermentation have been employed in exopolysaccharides extraction [39, 48], and these are: Solid State Fermentation (SSF) and Submerged Fermentation (SmF). The substances produced in the process of fermentation vary from species to species, and to a considerable extent influenced by prevailing environmental conditions. Antibiotics, preservatives (organic acids), pigments, enzymes, hypercholesterolemic agents, and antioxidants are a few of the natural bioactive substances reportedly produced through fermentation processes [49].

3.1. Solid State Fermentation (SSF) technique

Solid State Fermentation is a biotechnique that utilizes solid-based substrates for the extraction of substances and growth of microorganisms and mushrooms. These include bran, bagasse, paper pulp, chicken feather and agricultural wastes. These substrates are utilized slowly and can be maintained for over a long period of time with limited mechanical input. This has consequently afforded the SSF process the advantage of partial application in the bioconversion of wastes into value-adding products or waste management of organic agro-residues. While data remained scarce on the quantitative turnout of this technique in Africa, the application has recorded increase in commercial mushrooms production and given impetus to the expression biofuel generation in the African continent. Other bioprocessing applications such as bioleaching, bioremediation, biodegradation, biopulping and biobeneficiation were linked to SSF and are common in industries. While a wide range of microorganisms have been evaluated and confirmed to have potential in SSF, results have proven fungi, especially the filamentous fungi as the most amenable candidate for SSF. The process of production of bioactive substances from a fungus involves their inoculation into a solid substrate while controlling the appropriate physical growth conditions to mimic its natural ecological niche. The fungus develops fruiting bodies from which the substances are then produced. However, SSF process targets the extraction of materials of industrial relevance but has a few disadvantages popular among which is the turnaround time of the process, and difficulty in maneuvering yield, optimization and products purification. SSF is also relatively labor-intensive in addition to the substrate choice which exerts a stronger influence on the target product yield and optimization [50, 51, 52].

3.2. Submerged Fermentation (SmF) technique

This utilizes liquid substrates for fermentation at both laboratory and industrial scales. These substrates must contain the right amount and mix of nitrogen-carbon sources as well as other additives (minerals and vitamins) that may be required for energy generation by the target microorganisms. It is observed to be a more sensitive fermentation technology compared to the SSF. This might not be unconnected to the extra-methodological attention required for the appropriate timing of fermentation and aeration relative to the growth strength of the cultured organisms, treatment, and disposal of residual wastes [39]. Soluble sugars, fruit, vegetable juices, and sewage or waste water are typical examples of substrates that can be employed for SmF technology [5, 49]. The method is suitable for microorganisms that require high moisture content unlike the SSF process that involves near absence of free water. While SmF may arguably predates SSF based on historical annotations, it is evidentially popular in the continent since antiquity for the production of diverse soured milk products, alcoholic beverages, fermented foods (pastes, fruits and cheese) and flavoring agents. The mode of application of this technology varied with indigenous local tradition and food heritage. SmF technique has several advantages that may include a high yield potential for mycelia or spore production, fewer chances of contamination, and ease of product purification [50]. Easy manipulation of growth factors [13, 14, 53] and nutritional requirements [54] for small and medium scale production maneuverability, and long mycelia storage duration without alteration of genetic integrity accounted for the attention given to this method [52, 55]. The outcome of the fermentation process depends on the metabolic capacity of the microorganism, growth nutrients, and physical conditions such as pH and temperature. An uncommon green approach involving mild alkaline and acidic treatments may be used for the extraction of mycelia exopolysaccharides [46, 56, 57].

4. Structural elucidation and influence of bacterial and fungal exopolysaccharides

Exopolysaccharides of bacteria and fungi are widely relevant as they are versatile with application in food, agriculture, environment, health, and economic development strategies. Historically, fungi ranked among the earliest reported sources of valuable exopolysaccharides and their use for commercial isolation dates as far back as 1811, long before the discovery of dextran in *Leuconostoc mesenteroides* in the mid-19th century [20, 58, 59]. The growing application and improvement of EPSs for specific activity as demanded across the world is facilitated by the identification of varied sustainable alternative sources requiring simple, inexpensive, benign isolation, and purification strategies. Characterization of a particular exopolysaccharide is consistent with identifying the anomers (if any), monomeric units, the type of linkage between the monomers, and the linkage sequence. Methylation analysis is a tool used in knowing the monomeric linkages present in EPS [9]. Sequencing techniques include mass spectrometry and Nuclear Magnetic Resonance (NMR). NMR technique is used in determining the 2 or 3-dimensional structure of oligosaccharides [60]. While there is no clear understanding of how the difference in the chemical classes of EPSs impact their respective functionality, one can infer that the sequence of organization of EPSs' repeating unit and position of chemical functional groups encoded by genetic mechanism is vital to predetermining their potential bioactivity, ecophysiological functions, desired rheological and physicochemical properties. In addition, the appropriate application of EPSs in different areas of human life is dependent on certain expressed characteristics which according to Kaur and Dhillon [57] may include: (i) easy predisposition to biochemical modification to yield diverse processed forms e.g powder, gel, flakes, sponge, etc; (ii) possession of polycationic and biodegradable properties [45, 61]; (iii) physical and chemical resilience; (iv) must be innocuous with high degree of deacetylation, and free of impurities (heavy metals, protein residues). These differentiate biopolymers from petrochemical-based polymers commonly used in some developing nations in Africa. Consequently, active manipulation of the biopolymers structure through various bio-engineering techniques for a novel activity or compatibility with other biomaterial for industrial and biomedical applications is gaining attention globally.

4.1. Exopolysaccharide sources, products and applications

Exopolysaccharides are exploited from both bacterial and archeabacteria sources [8]. Dextran, xanthan, and gellan gum are three common exopolysaccharides produced from these prokaryotes (Table 1).

Table 1. Bacterial sources of EPS and their nomenclature.

EPS Type	Configuration	Units
Alcaligenes faecalis	Curdlan	[70]
Paenibacillus polymyxa, Bacillus lentus, Microbacterium laevaniformans	Levan	[71]
Pseudomona elodea and Sphingomonas paucimobilis	Gellan Gum	[8]
Halomonas maura	Mauran	[72]
Leuconostoc mesenteroides	Dextran	[8]
Xanthomonas campestris	Xanthan	[8]

Thermophilic bacteria such as *Bacillus thermantarcticus* and *Geobacillu sthermodenitrificans* are also reported as competitive producers of EPS. Exopolysaccharides occurs in thermophilic and halophilic archaea such as *Thermococcus*, *Sulfolobus, Archaeglobus fulgidus* and *Thermococcus litoralis* respectively in the form of surface biofilm [62]. The myxobacteria produce an enormous variety of polysaccharides primarily for locomotion, protection against phagotrophs and dehydration [63]. While it is still challenging for scientists to adequately determine which is the better source of extractable exopolysaccarides between fungi and bacteria (the better source of exopolysaccharides), fungi, based on their structural and cellular complexities are hypothetically perceived as superior reservoir of diverse polysaccharides. Mushrooms and endophytic fungi have been used in the past as dependable sources of useful industrial exopolysaccharides [17, 64]. *Phellinus linteus*, *Ganoderma lucidium*, *Fusarium* sp., *Pleurotus* spp. and *Inonotus obliquus* (Table 2) are representative examples of the vast array of fungi that have been exploited for exopolysaccharides [65, 66, 67, 68] (see Table 3).

Aspergillus fumigatus remains one of the most widely used conidial fungi for the production of galactosaminogalactan (GAG). Like the bacterial counterparts, some fungal pathogens of humans, notably *Candida albicans* and *A. fumigatus* also produce EPSs as biofilm during infection. This biofilm contains GAG, glucan, and galactomannan which influence its structure and function, mediates adherence to host tissue, aids evasion of the host cellular defenses, possess selective insusceptibility to fungicidal agents as well as enhance pathogenicity [69]. Furthermore, Orlandelli *et al.* [17] reported that *Diaporthe* sp. produced an exopolysaccharide that has 91% carbohydrate and 8% protein contents indicative of high-quality EPS.

Similarly, high Molecular Weight (MW) EPSs are observed to show more effective biological activity when compared to those with low MW. In other cases, the molecular weight may not be a critical factor in determining biological activity. Three-dimensional configuration of schizophyllan has been correlated with its antitumor activity. This further confirms the role of the chemical architecture of EPSs as defined by their branches, glycosidic linkages and molecular weight in their functional behavior. The molecular weight variations and sugar compositions of fungal EPSs are determined by the culture medium composition and the physical conditions of the fermentation process used in their production.

Extracellular homopolymers of glucose produced by fungi have applications in the food and cosmetic industries. Additionally, some fungal glucans of β (1→3; 1→6) and β (1→3) configuration possess anti-tumor, anti-inflammatory, and immunomodulation activities [1].

Exopolysaccharides in recent decades are gaining attention and exploited in multiple forms for use in many areas of human endeavors, including industry (textile, dairy, food and cosmetics), health (medicine and pharmaceuticals), the environment (remediation and flocculation), and in agriculture (preservatives, bioherbicides, microbicides) [82]. The various aspects of animal and human medicine including drugs (curative, prophylactic and antibiotic therapies), surgeries, biopsies, diagnosis and other systematic orientation are tempered with EPS and allied products. EPSs now rank among non-toxic natural products and other derivatives of biological resources with proven specific and non-specific bioactivity properties that are remodeling global medical treatment practices.

Dextran, produced by *Leuconostoc mesenteroides, Streptococcus*, *Lactobacillus, Gluconobacter* and xanthan from *Xanthomonas campestris* is a vector molecule [52] that delivers drugs to specific action target or tissue coupled with their role as natural anionic polyelectrolytes [83]. Exopolysaccharides have also been used as blood plasma extender, blood flow tonic, and anticholecterolics [84]. Furthermore, gellan derived from *Pseudomonas elodea* and *Sphingomonas paucimobilis* has a biomedical application as a placebo and in the administration of nasal formulations. Exopolysaccharides *Leuconostoc helveticus*, *Alteromonasinfernus*, *Leuconostoc paracasei* and *Rhodotorula glutinins* respectively were also documented to have antitumor, antioxidant antiviral and anticoagulating properties [84]. Some exopolysaccharides have been recorded to stimulate cell proliferation, and others have an anti-tumor effect. EPS has also been reported to induce positive physiological responses in humans while immunomodulatory activities have been associated with EPS produced by *Cordyceps sinensis*Cs-HK1 [85]. Schizophyllan from *Schizophyllum commune* has anti-tumor and immune-stimulating action. The macromolecule stimulates the immune system to fight cancerous cells while the sulphur modified schizophyllan has greater potential as an anti-retroviral remedy of Human Immunodeficiency Virus (HIV). Similarly, EPS from *Acetobacter xylinum* (BioFill) is tested as an implantable material in plastic surgery and has a number of potential uses including wound dressings for patients with burns and chronic skin ulcers [31]. EPS of *Phellinus baumii* has shown direct immune-stimulating activity on splenocyte proliferative response and acid phosphatase activity in peritoneal macrophages of mice.

Food has been essential for human wellbeing since the beginning of time in their natural or processed forms. EPS is imperative for food quality, manufacturing, processing, and preservation. EPS derived from lactic acid bacteria (*Leuconostoc, Streptococcus, Lactococcus, Pediococcus* and *Bifidobacteria*) are more commonly employed for dairy and fermented foods e.g.

Table 2. Fungal sources of EPS and their nomenclature.

FUNGI	EPS	REFERENCES
Botryosphaeria sp.	Botryosphaeran	[1]
Aureobasidium pullulans	Pullulan	[1]
Schizophyllum commune	Schizophyllan	[73]
Aspergillus fumigatus	Galactosaminoglucan	[69]
Candida albican, *Zygosaccharomyces rouxii,* Filamentous fungi	Chitin and Chitosan	[74] [75] [57]
Pleurotus ostreatus	Pleuran	[76]

Table 3. Chemical configuration of Fungal and bacterial EPS.

EPS Type	Configuration	Units	References
Curdlan	β(1→3)	Glucose (Glucan)	[70]
Levan	β-(2→6)	Fructose (Fructosan)	[70]
Gellan Gum	1,3-β-D-glucose, 1,4-β-D-glucuronic acid, 1,4-β-D-glucose, and 1,4-α-L-rhamnose	Rhamnose, glucuronic acid and glucose	[77]
Dextran	α(1→6; 1→3)	Glucose (Glucan)	[78]
Xanthan	β(1→4; 1→2; 1→3)	Glucose, mannose, glucuronic acid	[79]
Botryosphaeran	β(1→3; 1→6)	Glucose (Glucan)	[1]
Pullulan	α(1→4; 1→6)	Maltriose	[80]
Schizophyllan	β(1→3; 1→6)	Glucose (Glucan)	[73]
Pleuran	β (1→3; 1→6)	Glucose (Glucan)	[81]
Scleroglucan	β (1→3; 1→6)	Glucose (Glucan)	[1]

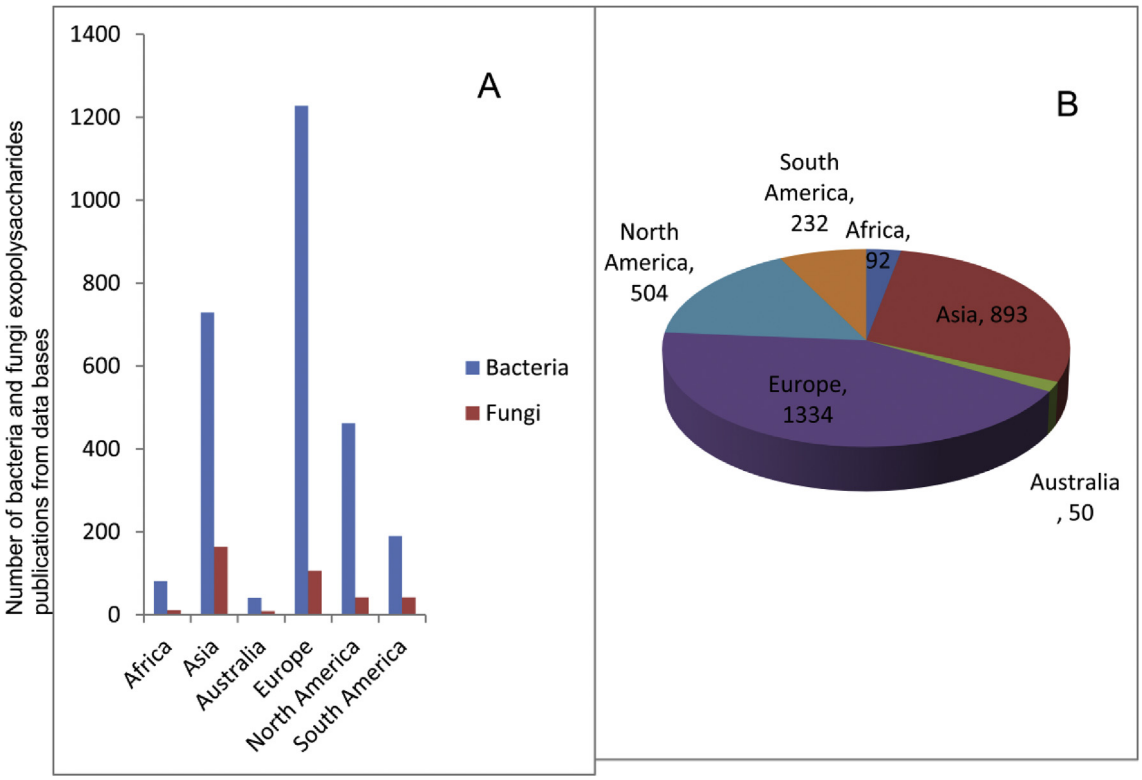

Figure 1. Global overview of exopolysaccharides' research profile (38,000 articles indexed in scopus. 1976–2018). A- Compared global exopolysaccharides' publication profile of bacteria and fungi; B- Global exopolysaccharides' publication profile.

milk, curd, sour cream, yogurt, cheese, buttermilk manufacturing to enhance the flavor, taste, texture and shelf-life of fermented foods [84, 86]. Additionally, dextran improves moisture retention in confectionaries, increases viscosity and sugar crystallization while xanthan and emulsan (*Pseudomonas fluorescence*) serve as a stabilizer, emulsifier, and suspensor or thickening agent respectively in various food industries. The incorporation of EPS in foods also alters the visco-electrolyte and rheological properties of the water present [31]. Pullulan from *Aureobasidium pullulans*, a fungus is also used as a thickener and viscosity stabilizer in the food industry [7]. Other industrial applications that involve the use of exopolysaccharides include paints, pesticides, ink, detergent and gelling agents for solidifying of culture media.

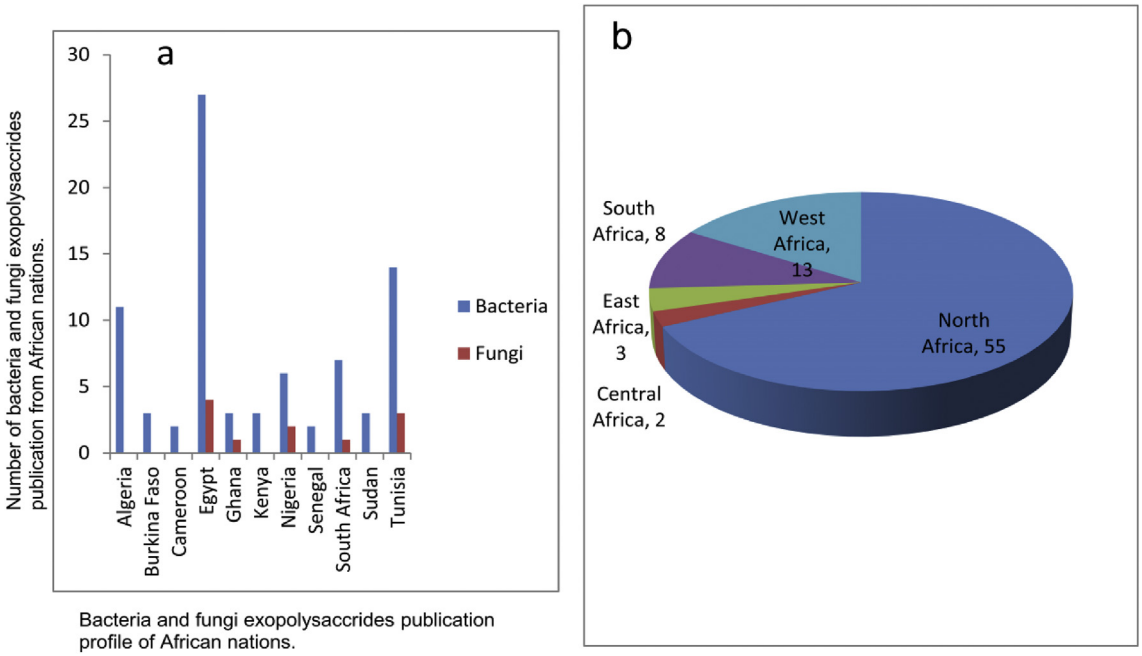

Figure 2. Overview of the orientation of bacteria and fungi EPS research and application in Africa a) countries rating, b) regional rating (81 articles indexed in scopus. 1976–2018).

4.2. EPS current status and perspectives in Africa

The recent paradigm for cost-effective, safer products for human needs has revolutionized the frontiers of research objectives. This has led to solving challenges of various regional and global dimensions with biotechnological approaches with variably impact on industries, pharmaceuticals, medicines, agriculture, dietetics, beliefs and conservation science. While the long-term consequence created by widely growing exploitation of nature's biogenetic resources for the production of novel products valuable to human welfare dominates scientific debates, the wide range effects of such on global evolutionary, ecological and anthropological dynamics remain rudimentary. Products of values derived from bacteria, fungi, algae, plants, and animals are perceptively acclaimed safer than synthetic products of chemical origin due to their innocuous effect on humanity and sustained mediation of target cells, tissues or microbes. EPS is one of the products of value derived from plants, fungi, algae, bacteria and recently from slimy animals. Plants and algae are more commonly exploited for EPSs and their by-products than other biological sources possibly due to their preponderance and accessibility. The dependence on plants and algae for EPS production is unmindful of their ecological relevance as primary producers and pivot of many ecological systems' balance, and exert pressure on the world food webs. This has recently stimulated research towards using non-photosynthetic bio-resources as raw materials for the production of EPSs.

A preliminary but random study of exopolysaccharides publications spanning 18 years period (2000–2018) from Scopus (38,000), Sci-hub (4,709) and PubMed (8,710) data bases was carried out. The rough estimates of literature on exopolysaccharides were used as surrogate data in evaluating the trend of African research and interest in EPSs. Since studies of this nature were seldom found in prints, we assumed that the data obtained on the subject of exopolysaccharides from top indexing repositories would directly reflect the current utility and economic

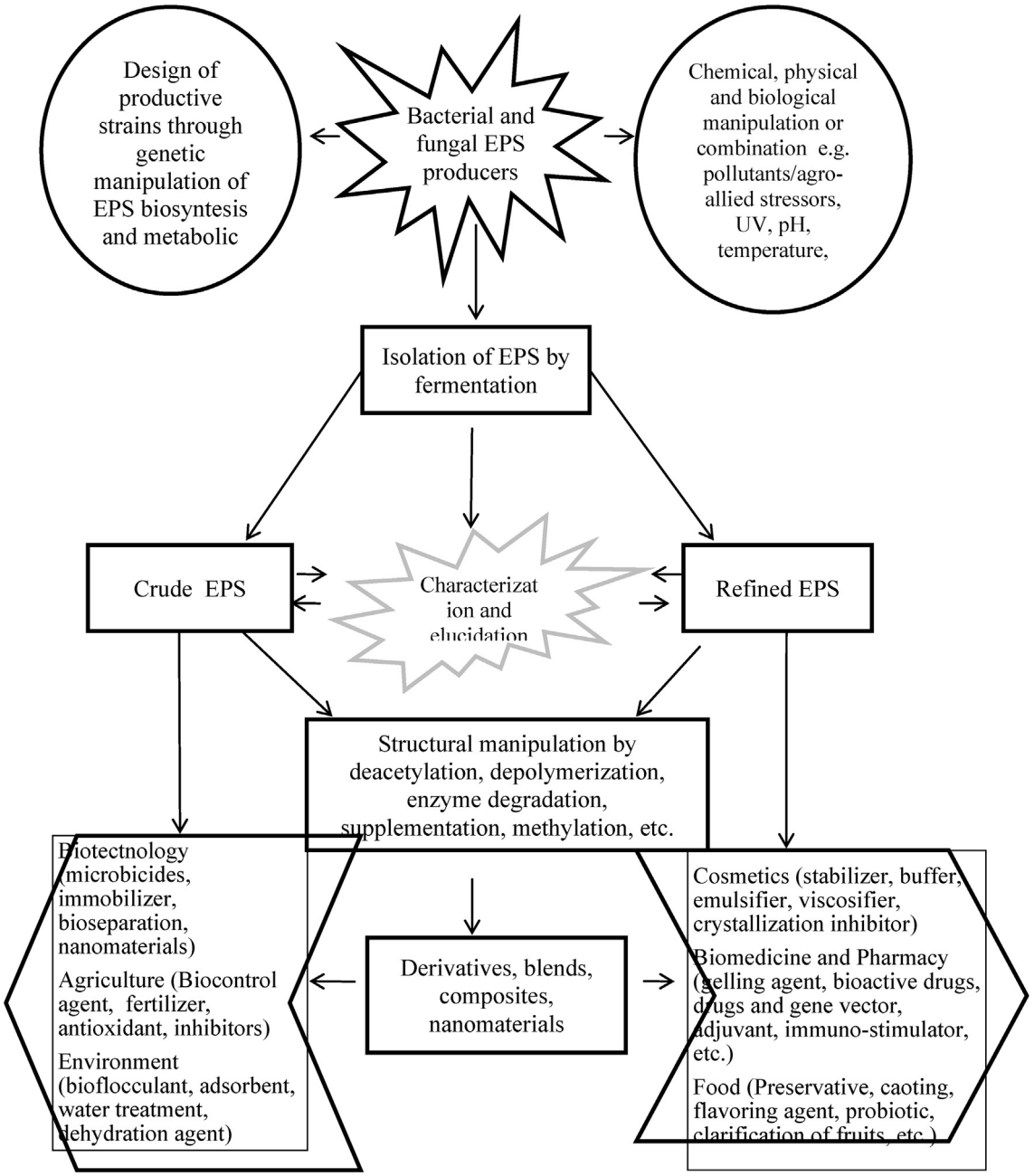

Figure 3. Simple schematic overview of EPS isolation, purification and products application.

dynamics of EPSs in Africa. While the study is not unmindful of the repetitiveness of articles by authors' affiliations across national strata and indexing data bases, using publications data on the subject of study would insignificantly distort the pattern and dynamics of EPSs' research and applications. Similarly, the data while acceptable for providing a snapshot of an African perspective on EPSs research proclivity, utility, economic and cultural dynamics, gave representations of EPSs derived from biological sources as well as synthetic (aliphatic polyesters and polyphosphoester) and semi-synthetic biopolymers. Scopus data base is used as the main reference for this study because it is the largest indexing repository with a global demographic spread. EPSs derived from plants, algae fungi, bacteria and animals in their diverse usable forms have been reported in literature [87] while methods for optimizing productions and isolating from these biological sources also abound in literature [16, 88]. Many scientific reports have associated the growing environmental and ecological concerns of the world to the over-exploitation of plants and algae, major primary producers, for several valued-products, including EPSs, needed for the improvement of humans' wellbeing. This within the last decade has resulted in a paradigm shift to other biological sources (bacteria, molds, yeast, and mushrooms) that are environmentally friendly, preponderant with spontaneous reproductive cycle, and high yielding for industrial-scale production of EPSs. Bacterial and molds have now been reported as competitive bio-equivalent sources of EPSs which when subjected to compatible bioreactor technology has the capacity for industrial-scale yield. To what extent then has the continent of Africa contributed to the global biopolymer market? Where exactly does Africa stand in bacterial and fungal EPS researches and their deployment to economic welfare?

About 38,000 pieces of mostly journal articles on EPSs which were spatiotemporally distributed across different time, disciplines and geographic locations were noted on the Scopus indexing data base. Interestingly, only 8.4% of these were related to bacteria (3, 10, 5) and fungi (85) EPSs out of which 97% were on bacteria-based EPSs. While these strongly projected bacteria species as the preferred alternative bio-source choice when compared to fungi for EPS production and research, it also corroborated findings from previous studies and indexing data bases e.g. PubMed (61%) and Sci-Hub (81%). The preferred choice of bacteria over fungi for medium and large scale biotechnological and industrial production of EPSs that are of competitive quality may not be unconnected with some of their pertinent characteristics. Some of these include rapid reproductive capacity which ranked them as highly renewable, biological plasticity that confer the ease of bio-engineering manipulations for quality and yield in EPS isolation, compatibility to various EPSs isolation techniques with simple purification requirement and human ethological propensity to control bacteria and their obnoxiousness [13]. Biopolymer researchers' attraction to bacteria suffices as a partial control of the bacterial population and human exposure to their clinical challenges. Research information from Africa on EPSs of bacterial and fungal origins constituted about 3% of the global biopolymer reports indexed in Scopus, only rated above Australia (Figure 1). The underdeveloped use of EPS research output as measured by this result for the African continent may be attributed to a number or combination of factors that include (i) ignorance of the biotechnological and industrial applications or relevance of the compounds, (ii) dependence on other alternative analogs or bioequivalent sources of EPS, especially plants and animals, for the fulfillment of domestic, commercial, industrial and pharmaceutical needs, (iii) lack of political will for funding adequate, research, technology or technical know-how required for the exploitation of EPSs from the luxuriant preponderance of continental bioresources, (iv) inadequate economic development plans by nations and governance improprieties. It is vital to note further that publications on EPS hoisted on scopus data base credited to African authors were temporally and spatially far-in-between. The low number of articles over the period reviewed could be traced to related works by Africans in diaspora not credited to institutions in African and possibly contributions by African EPS research community published in non-scopus data bases. Interestingly, Africa ranked lower among the league of continents (Europe, Asia and South America) and nations (China, Brazil, India, USA, France) dominating bacterial-fungi EPSs applications and research landscape respectively.

In Africa, less than 15 nations from the 55 recognized by the African Union were identified to have research orientation in bacteria and fungi EPSs with Egypt leading the pack of African nations with EPS biotechnology, research and industrial tendencies (Figure 2). A total of 98 articles in scopus data base was noted, 17 of which were attributed to authors in the diasporas but credited to non-African nations. The reason for the observed trend is not yet fully understood but may be strongly correlated with the state of national vegetation, culture and economic development from industrialization and technology perspectives, and the level of political stability as well as literacy. It is also logical to assume that demographic dependence on bacteria and fungi was forced by poor forest vegetation which left little bioresources choices, particularly algae and plants, for EPS production. Furthermore, fungi are reported to be the priority choice for the best quality chitin and its derivatives but remained unattractive for industrial-scale production of EPSs for reasons contradictory to the aforementioned [59, 82, 89, 90, 91]. Similarly, domestication of valuable species of fungi, especially mushrooms, for human industrial and welfare needs in many African nations is still rudimentary and oriented at solving hunger challenges [7].

5. Conclusion

Exopolysaccharides hold great promises in different areas of human endeavors far more than presently imagined (Figure 3). Undertaking, on a preliminary scale, a study of this simple nature that involves usage frequency of articles on Scopus data base and other related indexing repository as surrogate for measuring the research trends, spread and utility of EPSs as well as their derivative (blends, composites or nanomolecules) is unique and novel. Attempts have been made to identify varieties of natural EPS and their sources [20, 58, 87]. Also, further studies exist on their physicochemical as well as rheological properties purportedly for understanding best maneuverability that gives their optimal production [15, 22]. Globally, the value placed on EPS market and commercial applications is stimulating rapid development of research into newer strategies for their sourcing, production, isolation, purification and reconstruction into functional derivatives. The gradual growth in biotechnological consciousness in Africa is revolutionizing the utility of diverse bioresources and the improvement of traditional food processing techniques was reported by Adetunji and Adejumo [93].

This review aimed at sensitizing and challenging African biopolymer researchers to explore the biotechnology orientated studies that afford utility opportunities of EPSs application for national development amidst other competing interests or militating factors. It also subtly investigates the Scopus indexed research orientation of African researchers while encouraging Africans in diaspora to dedicate related studies to the development and recognition of Africa. The low level of research publication on EPS from African nations is a scientific measure of their relative affinity for the biomaterial. Consequently, the results clearly showed that many African countries are uninterested in the values afforded by EPSs as raw bio-materials in food, pharmaceutical, petrochemical and cosmetics industries even though they are reportedly used as preservative, stabilizer or confectionary, crystallization inhibitors, biosulfactant, thickeners, adsorbent, buffers, insulators, emulsifiers and gelling agents [3, 6, 84]. Karana *et al.* [15] have also implicated EPS of fungal mycelia in material design. The Scopus list of bacterial and fungal EPS-related publications from Africa suggested a late start (2002) in EPS research and application. Some examples of African nations represented in EPS biotechnology and bio-engineering on Scopus within the period investigated include Algeria (2005), Ghana (2012), Burkina Faso (2004), Cameroon (2004), Egypt (2004), Senegal (2017), South Africa (2016), Sudan (2008) and Tunisia (2006). This appeared to be inconsistent with

the observed global trends as mostly exemplified by many developed countries. Impressively, North African nations and researchers have shown better commitment to bacteria and fungi EPSs than do other regions due to possible proximity to Europe and trans-border technology exchange. Further investigation may be required to understand the influence of vegetation, political, sociological and economic dynamics, and culture in stimulating EPSs research, exploitation, utility and need orientations despite the observed correlation from this study. There is no doubt that EPS and its derivatives have promising potentials that could be explored for diverse gains, including national and foreign exchange benefits through engaging global biopolymer market. The review further aims at improving knowledge on the industrial and non-industrial versatility of EPS and boost imagination on how their rapidly evolving applications could extend to solving the portable water, healthcare, and food challenges in Africa. This therefore validates the perceptions that Africa is endowed with unlimited biological resources, including archaea, most of which are yet untapped but with promises of being ranked as one of the best repository of EPSs in the world [92, 93]. It accords researchers of African origin the opportunity for improved research report representations in the world's recognized abstract indexing data bases and opens up fresh avenues for novel discovery of EPS isolation and optimization strategies.

Declarations

Author contribution statement

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Competing interest statement

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Additional information

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