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Chemistry of Natural Products Current Developments and Future Directions

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ABSTRACT

By providing novel applications, constructive inputs, thrust, comprehensive understanding, broad perspective, and a new vision for the future, natural products chemistry lays out its role and contributions to the advancements of the physical and biological sciences, its interdisciplinary domains, and the emergence of new avenues. As part of the current review of the basic and core developments, innovation in techniques, advances in methodology, and potential applications with their effects on the sciences in general and natural products chemistry in particular, the future prospects in bio-medical, health, nutrition, and other interrelated sciences are also discussed, as are some emerging trends in the subject area. Natural products chemistry is discussed in terms of its historical history, its present-day role and economic and scientific ramifications, and its future aspirations, prospects, and aims. The role of natural products chemistry in advancing research in a wide range of fields is discussed.

An Overview: Origins, Effects, Range, and Influence

Because of their widespread influence on science, technology, and the economy, natural products and natural products chemistry have recently experienced a renaissance. The focus is back on track after the topic nearly lost its luster. The decline of interests due to lack of prioritization, non-availability of precise tools and techniques with resulting inhibition, lack of interest, unavailability of upgraded analytical tools, and lack of wider academic and industrial programs along with the poor financial resources for advancements and research and developmental opportunities for new discoveries and applications impacted the (i) advancement of knowledge in understanding of physical and biological science avenues and its interrelation of wider disciplines with economic impacts, (ii) progression of technological advancements, especially in analytical, biotechnical, and pharmaceutical domains, (iii) importance, outreach, and the discipline's role as a tool of modern research into chemical sciences for its broader applications, and (iv) later advances in mechanistic of natural world's biotic and abiotic processes, environment and ecosystems with their natural products, metabolites, and the involved chemistries, all impacted the discipline. Purifications, characterization, structure determination, functions, inter-relational chemical and metabolic dynamics, and vigorously diverse characteristics and pharmacology-based usage and roles led by an understanding of natural products and their chemistries have streamlined the advancements in the further understanding and contributions to a field that is experiencing unprecedented growth in terms of knowledge of the more common natural products. Developmental prospects for greater specificity and more widespread applications in the chemistry of terrestrial species and marine organisms were expanded by the discovery of the finer details in the ecological settings and impact on the generation of the constituents of natural resources, as well as its variations in design and diversification (Atanasov et al., 2015). Although modern methods have had a substantial effect on phytomedicines, synthetic chemistry, purification method development, ecological comprehension, agricultural sciences, the chemo-environmental outlook from the perspective of natural products, and related technological advances and economies, there is still room for improvement. Intricacies of the topic have been further revealed by our improved understanding of microbial chemistry, plant-microbe interactions, metabolite biogenesis, the significance and elicitation of secondary metabolites, symbiosis, and photochemistry. Natural products chemistry is developing into a chemical instrument to understand the biological aspect of natural resources and their chemistry, biology, ecology, and environment as a result of the understanding of the functions of the evolutionary-interrelated biosystems, the developments and expansions into spheres that encompass inter-relational science areas for the natural products chemistry, chemical biology, systematics, and metabolic engineering. Additionally, the utilization of natural product resources, product development, raw material sustenance, and future action planning were all influenced by the divergent perspectives held by academia and industry (Amirkia and Heinrich, 2015). Natural products discovery efforts, such as new medicine discovery, were stymied due to bottlenecks in approach, methodology, and design for sustainable use of resources due to growing perception gaps between academic and industry specialists. The lack of proper technical means and other analytical tools, and probably the resultant de-motivation for solving the encountered problems in natural products chemistry research due to shortcomings in applying the existing knowledge to its maximum use, dampened the resolutions of intellectual inquiries over time and across locations. Multiple factors, including advances in technology and techniques, funding, support, and sponsorship, have contributed to a slower-than-desired evolution of the field and its underlying disciplines (Li and Vederas, 2009). Despite this, there has been an increase in the use of marine templates and marine drugs like marrubium as well as interest in ethnobotanical herbs and nutraceuticals; discoveries and understanding of chemical ecology and systematics; human genome profiling; the search for therapeutic templates for the chronic and genetic diseases; details into biomechanics, biogenesis, and templated biosynthesis; and the interest in marine templates and marine drugs. New chemical entities and target templates for structurally and pharmacologically diverse bioactive compounds have been significantly aided by the recent debates on priorities and reports of natural products isolation from contrasting bio-diversified areas (Fitzpatrick, 2004, Bull, 2003), identification of the active constituents of traditional remedies (Mollo et al., 2015, Oberlies et al., 2003), and the search for new compound-templates (Banerji, 2000).

Natural products have been shown to have a high problem-solving potential (de Smet, 1997; Berman and Flanery, 2001; Kayne, 200); this is because of their ability to identify structure, function, reactivity, and pathways; to generate synthetic routes via retro-biogenetic concepts; and to provide answers to other chemical challenges in the fields of phytochemistry, marine chemistry, chemical ecology, microbial chemistry, functional biochemistry, and macromolecular chemistry (Table 1).

Table 1Break through and contributions made possible by natural products chemistry

Drug discovery & development, semi-synthetics	Drugs and other medicaments started with herbal origins, majority of drugs before advent of synthetic drugs, feasible and cost-effective approach to drugs synthetic origin, contemporarily ∼50% drugs of natural origins, new templates design and new chemical entities being continuously discovered
Chemical synthesis	Retro-approach to biogenetic synthesis, total synthesis in a bio-mimetic patt routes, new templates, and challenging molecular frameworks availability
Therapeutic agents	Taxol, Cephalosporins, Penicillins, Tetracyclines, Camptothecin, Etc Podophyllotoxin, Combretastatin, Homoharringtonine analogs, Marine Bryostatins, Ecteinascidin, Kahalalide F, etc.
Bioactives	Insect-repellents, herbicides, natural pesticides, larvicidal, auxins, phyt antihelminth, anti-filarial, neuro-active, cardiovascular, anti-hyperlipidemi protective, anti-inflammatory, anti-microbial, anti-cancers, anti-oxidants, anti-c pain-killers, anti-spasmodics, digestives, purgative, anti-ulcers, aphrodisiacs anti-allergens, etc.
Economics	Developing world economy, economic up gradation in plant resource-rich natior imports, in-house native consumption, forest-economies, long-lasting sustenanc
Pharmacopoeias, medical treatise, and alternative medicines	Ayurveda, Unani (Greco-Arab-Indian), Chinese as major plant-based healing African, Shaman, Red-Indian and other ethnobotanical medicinal usage tradit treatise. Aromatherapy, Homeopathy, and Siddha systems of medicinal usage
Consumables	Plant Pigments, Dyes, Essential oils, Fatty Acids & Lipids, Raisins and Gum, Ar Alkaloids and Tannins, Neutraceuticals, Spices, Condiments, etc.
Plant-based drugs of abuse	Hallucinogens, Narcotics, Cannabis, Opium, Semi-synthetics derivatives thereo
Technical products, fibers, and plant polymers	Jute fibers, Paper, Paper-boards, etc., Pectins, Alginates, Cellulose, Marine Products, etc.

Treatments and their Development

Natural resources have played an important role in the advancement of the field due to the interest in their pharmacologically active constituents, structural diversity, and synthetically challenging templates for development towards medicinal uses that have an impact on the broader pharmaceutical interests and related economic activities. Development of new techniques in separation, purification, and characterization of ligand-bound and free substrates,

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generation and establishment of test scaffolds, and the rush for small molecules drug discovery from templates and designs based on bio-diversified as well as chemically diversified natural products pools (O'Keefe, 2001; Mabry, 2001) have all contributed to the progress of isolating drug templates and newer drugs from terrestrial and aquatic sources as the reservoir of natural products. Again, the acquisition of chemo-biological products for medicinal uses, the rapid scientific progress in the applications in the technological domain, and the evolution of better methodologies, all of which have an impact on economic potentials, have significantly scaled up the static and regressive periods of interest in natural products, particularly for the agrarian societies, thereby serving as a tool of education, innovation, and economic growth (Harvey, 2010; Butler, 2011).

In addition, chemists now have new opportunities and problems in drug development and other health product discoveries thanks to the traditional herbals' reputation in ethnobotany and ethnopharmacology (Tan et al., 2015; Azam et al., 2016). Recent interest in natural products has yielded numerous interesting results (Cho et al., 2008, Qureshi et al., 2016), including the phenotypic and virtual screening based advances (Chang and Kwon, 2016, Shaikh and Siu, 2016, Cao et al., 2013) and it also saw a number of diversely-sourced products' remarkable discovery with antimicrobial (Moloney, 2016), anti-inflammatory (Bezerra et al., 2013), anti-helminth (Das et al., 2010, Mali and Mehta, 2008), anti-diabetic (Zhu et al., 2013), and anticancer activity especially taxol® (paclitaxel), anthracyclines, Vinca alkaloids, camptothecin, podophyllotoxins, epothilones, enediynes, combretastatin, homoharringtonineanalogs, marine-sourced bryostatins, ecteinascidin, and kahalalide F (Fig. 1) among several other natural products at various stages of development as anticancer agents (Kinghorn et al., 2009) leading the mainstream pharmacy's acceptance of the natural products as part of modern and practical tools for new drugs, and new drug discovery templates' reservoir (Von Nussbaum et al., 2006, Molinari, 2009, Butler, 2004, Quality, 1998, Hagino, 2000, Fauzi et al., 2013a, Donia et al., 2011a, Conforti et al., 2008). Currently, anticancer drugs derived from natural sources account for 60% of successful leads, whereas synthetic leads account for 40%.

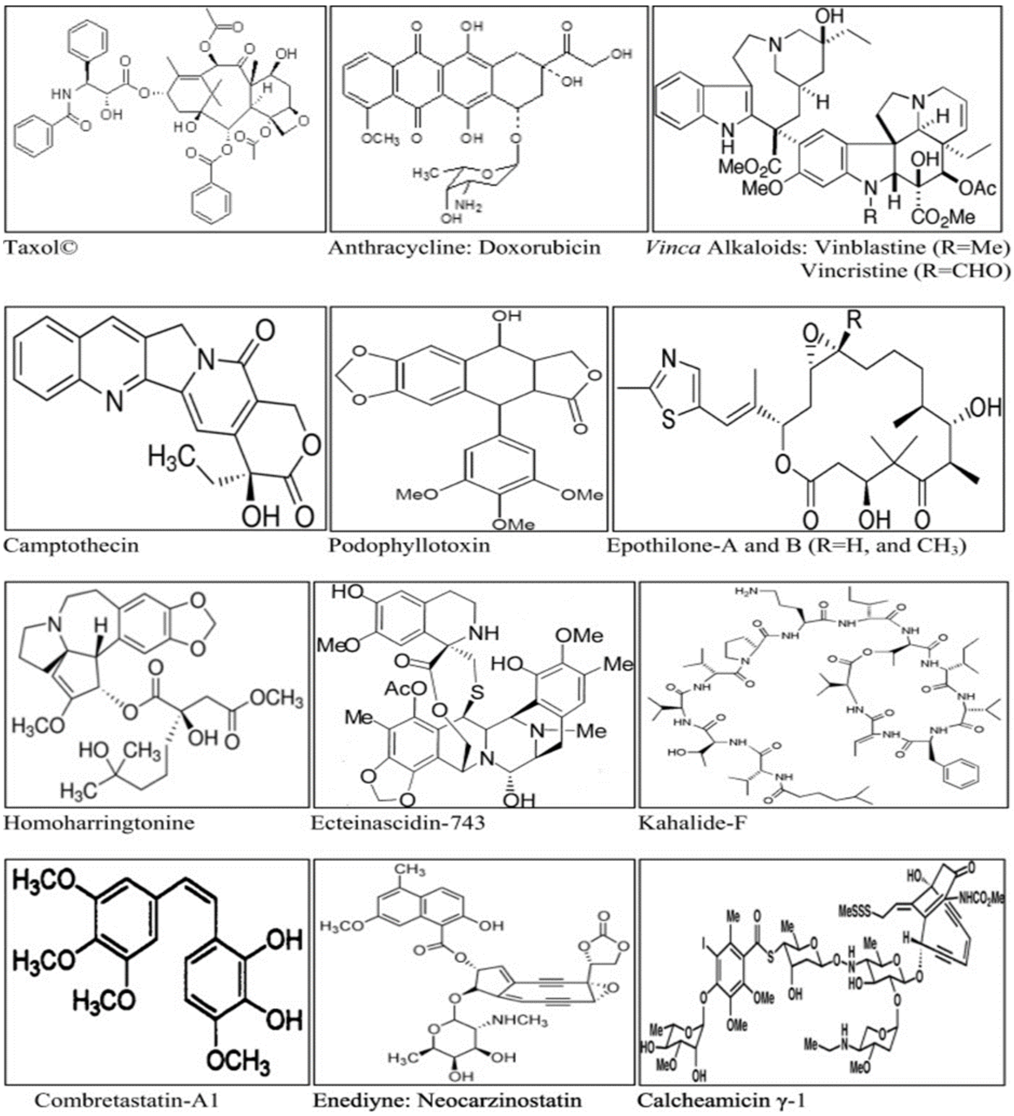

Fig. 1 The chemical make-up of a wide range of naturally occurring substances

The perspective of natural products is revaluated, in particular for the highly debated biological activity of single components versus multi-component products from plant(s) with or without the synergistic bioactivity profile, as well as the trace of no-activity or the watered-down biological activity of natural products of secondary metabolite's origin in drug-template screening versus the bioactivity due to the presence of high molecular weight non-polymeric, conjugated/clustered molecules.

Drugs That are Entirely or Largely Artificial

The introduction of synthetic chemicals as pharmacological agents established the groundwork for contemporary pharmaceuticals and drug research. Up until the 1980s, more than a third of medicines were derived from natural components. About half of all pharmaceuticals now come from synthetic sources, while the other half are primarily derived from natural resources. However, the development of drug templates for various biological activities, claims of adverse effects and perceived toxicity, the need for more sophisticated facilities and infrastructure, and compliance with stricter regulatory mechanisms have all contributed to the steady expansion of phyto- and marine-sourced drugs. Combining synthetic methods with pharmaceuticals and drug templates derived from natural sources has been a driving force in the field of natural products chemistry in recent years. Multiple research groups and institutions from across the world participated in the exercise, realizing the interdependence, molecular interconnectedness, and structure-activity relationships (SAR) for several natural templates, especially anticancer and anti-biotics pharmaceuticals (Lal et al., 2013). Natural items seen as preventative agents as nutraceuticals, food supplements, herbal medications, or complementary and alternative therapeutic agents have begun to reconfigure their appeal and perception, although not until lately in large portions of the world. As a result of the mild to severe negative effects of synthetic pharmaceuticals used to treat hereditary, lifestyle-acquired, occupational, and other chronic disorders, the search for safer and more effective drugs derived from natural sources became a viable option. Natural products, which were used by a large proportion of the world's indigenous peoples as medicine, offered a chance to investigate these medicinal resources and gain insight into their potential for further development through a systematic approach to bio-assay guided fractionation and activity location from the active constituent(s).

In addition, semi-synthetic analogs of natural products aimed to improve the current drug-like properties for biological activity by meticulously changing the structural features with inputs from SAR and QSAR, with or without disrupting the beginning molecular template. This allowed for the comparison and prediction of the original natural product templates to generate a new biological activity in the redesigned entity, with the help of in silico activity predictors. In addition to their known biological functions, natural products have been used as a practical starting material to generate substances with improved and new therapeutic efficacy (DeCorte, 2016, Banwell, 2008, Galloway et al., 2009, Kombarov et al., 2010, Tanaka et al., 2009).

Distinction and Structure Explanations in the Sciences

The development of more precise methods of separation, assaying, and detection has greatly aided the study of natural products. Stable and chemically non-reactive isolation and purification methods (Kloss et al., 2013, Donia et al., 2011a, Schmidt and Donia, 2009, Freeman et al., 2012, Taylor et al., 2007, Tianero et al., 2012); with improved technologies led to the discovery of minor-yield products on an unprecedented scale. Some of the more difficult aspects of isolation chemistry have been identified by researchers (Bedir et al., 2002; Khan et al., 1996). These include the presence of a complex mixture of secondary metabolites; molecular associations; a mixture based on polarity; preservation by the surroundings of biological molecules; ionic and non-ionic interactions and deposits (especially in marine products); chemical conjugation; and physicochemical phenomena. Bio-diverse natural resources and products were investigated for novel structures and bioactivities using analytical methods established for isolating and determining their structures (Berkov et al., 2014). Many problems with detection, isolation-purification, instant constituents screening or dereplication, and chemical profiling have been solved thanks to the development and increased use of non-traditional chromatographic techniques like Flash®, UHPLC (Ultra High-Pressure Liquid Chromatography), MPLC (Medium Pressure Liquid Chromatography), Electrokinetic chromatography, droplet counter current, super-critical fluid, and circular chromatographies, as well as gel filtration.

The substances in the chromatographic fingerprint can now be reliably identified thanks to a recently developed neural-network-based descriptor model for predicting the chromatographic sequence of natural compounds in a gradient chromatographic technique (Hou et al., 2016). The use of spectro-analytical techniques such as mass spectroscopy in conjunction with other hyphenated techniques like GC-MS, LC-MS, LC-DAD-TOF-MS (Luzzatto-Knaan et al., 2015, Wolfender et al., 2006), circular dichroism, NMR, and NMR-based correlational spectroscopies has altered the method of structure determination.

There has been a recent uptick in research into the purification and identification of active ingredient(s) from aggregated, molecularly clustered, conjugated, and physicochemically bound natural products in the field of natural products isolation, which encompasses the chemical processes involved in isolating substances from terrestrial, marine, and microbial products. On a wider scale and with greater complexity problem-solving capabilities, the demand for faster and more efficient approaches to separate and describe more significant hetero- and homo-polymeric molecules of natural origins from various sources appears increasingly imminent.

The use of Combichem and HT tests

It appears that a combinatorial or near-combinatorial approach in the biogenetic scheme of production is indicated by the naturally templated biogenesis on the chosen molecular framework, especially for the larger and repetitive units like tannins, biopolymers, and small molecules (with different substitutions also). The chemical characterization of prokaryotic organisms' products makes this phenomena more evident. The drug-like properties of many natural products within a single species and the templated and library-like synthesis of the most powerful natural ingredient were observed. Purified natural products libraries can be thought of as part of the combinatorial setup (Clardy and Walsh, 2004, Koehn and Carter, 2005, Tianero et al., 2012, Pelish et al., 2001) to discover the increased biological activity and pharmacological diversity for further development of the hit template. The folding, branching pathways, and oligomer-based approaches developed for the synthesis of skeletally diverse small molecules have been reported in diversity-oriented synthesis and combinatorial libraries of natural product-like substances (Koehn and Carter, 2005; Trabocchi et al., 2013; Singh and Culberson, 2009; Galloway et al., 2009). Several studies have reported the combinatorial synthesis of natural products based on, and natural products like molecules, bacterial and fungal origins constituent's templated molecular frameworks (Davis et al., 2007, Georgiades and Clardy, 2008, Tanaka et al., 2010, Olano et al., 2010, Behnken et al., 2012). This has increased the reach and utility of natural products chemistry.

High-throughput (HT) screening of the crude extracts, as well as the use of various analytical techniques for purified natural products and natural products-based combinatorial libraries for template selection (Poulsen et al., 2006, Frearson and Collie, 2009), show promise for future applications. In addition, false leads caused by pan-assay interference compounds (PAINS) were separated from a large pool of synthetic and natural products using data from high-throughput screening (HTS) and an existing database (NAPRALERT). These products had displayed multiple bioactivities that were inconsistent with the characteristics of the synthetic libraries and were thus labeled as invalid metabolic panaceas (IMPs). Nearly half of the 200,000 products analyzed exhibited power law features, yielding a hyperbolic black hole in the occurrence-bioactivity-effort space in which IMPs populated the high-effort base (Bisson et al., 2016; Georgiades and Clardy, 2008).

Mechanisms and Biological Function

The chemical biology method has been a useful tool for elucidating the finer biomechanics of traditional medicine's effect. The pharmacophoric model of bioactivity exhibition has been refined, and its use has enabled the outlining of the mechanism's competing and synergistic constituents, targets, and routes. The mechanistic specifics aided in the comprehension of creating remedies for complex diseases (Bai et al., 2016). Downregulation of specificity protein 1 (Sp1), Sp3, and Sp4 are highly expressed in malignancies, and the anticancer drugs and their analogs work on multiple pathways; one novel approach proposes targeting the Sp transcription factor. Sp-regulated genes are thought to play a role in a variety of cellular processes, including proliferation (cyclin D1 and growth factor receptors), survival (bcl-2 and survivin), angiogenesis and migration (MMP-9, vascular endothelial growth factor and its receptors), and inflammation (NF-kB), both in tumor cell lines and in primary tumors. The clinical applications of natural products and their combination medications may be further optimized by confirming the precise biomechanics (Safe and Kasiappan, 2016). Several flavonoids, including myricetin, quercetin, and epicatechin, were tested for their ability to inhibit aldehyde oxidase (AO), an enzyme responsible for the biotransformation of drugs and xenobiotics, in an in silico model and in vitro (Hamzeh-Mivehroud et al., 2014). In HeLa human cervical cancer cell lines, the flavonoid lutein was found to prevent cancer growth by blocking the PI3K/AKT/mTOR pathway. Tumor development was inhibited and oxidative stress was decreased because it boosted ROS generation and decreased phosphorylation of PI3K, AKT, and mTOR expressions (Bai et al., 2015). The antitumor activity of Hypericum hookerianum (Dongre et al., 2008), polyketide inhibitors of eukaryotic protein synthesis (Taylor, 2008), and other recent reports all highlight the importance of biomechanics in evaluating the bioactivity of the natural compounds.

The influence of the Genome's

Understanding the fundamentals of disease requires access to genomic data. However, developing effective therapies requires precise diagnosis and identification of causes by proven biomarkers in order to zero in on the underlying entity or function at the root of the problem. This is true for our own genome as well as any other genome. In this respect, the sequence data from the human genome must be translated into a variety of step-by-step responses in order to contain and heal specific cells, tissues, organs, and diseases. In order to confirm the central and peripheral activities mediated by genomics, it is necessary to mine the data and use it as a judge in receptor-ligand binding studies, mechanism of action and bioactivity, site-directed drug administration, and other investigations. Small and large molecules as bioactive components filling the disease versus natural products interaction gap(s) with the aid of the natural product probe-compounds (Siegl et al., 2010; Schmidt et al., 2004; Partida-Martinez and Hertweck, 2005; Kwan et al., 2012; Kroiss et al., 2010; Walter et al., 2011; Fauzi et al., 2013b,53); these This knowledge could also be used to develop more effective templates and inhibitors or boosters of bio-functions for a wide range of applications. Genome-based natural product discovery has been reported (Franke et al. 2012; Hentschel et al. 2012; Banskota and McAlpine, 2006), and genomically identified and enabled targets may play a pivotal role in the future development of novel therapeutic medicines. Understanding the bacterial genome, gene expression, mechanism of resistance to antibacterial drugs, and the ability to succeed as a pathogen in human patients has led to promising advancements in antibacterial therapy

(Punina et al., 2015). The era of individualized therapy based on natural ingredients is behind us, but genomics is here to play a larger role.

Bioengineering, Fermentation, Enzymology, and Synthetic Biology

Cell suspension culture-based products and their variants (Davidson, 1995), symbiotic conditions and their products (Tse and Boger, 2004, Pidot et al., 2014, Moore et al., 2002, Schmidt, 2005, Schmidt et al., 2005, Wilson et al., 2013, Peraud et al., 2009, Nützmann, 2010), and the identification of fermentation broth compounds. Studies into the structural and physicochemical property modulations in the enzyme and changes in the function and structural characteristics of the substrate (s) have begun to unravel in more detail the impact of enzymology in the use of large, medium, and small enzymes and enzyme-mimetic templates in relevant areas of chemistry, phyto, and other natural chemicals. Unlocking the secrets of biochemical bioengineering, which is currently being approached via broader natural products chemistry applications in enzyme, proteins, peptides, and peptide-mimics (Franke et al., 2013, Scharf et al.), hinges on the presence of diverse bio-molecular plant structures, response(s), and biochemical properties in defining the functional outlines and, if involved, product outcome from the biochemical processes, their reactions, Key to improving industrial operations to the following performance levels is the employment of enzymes and enzyme-mimetics in large-scale manufacturing, the design of protocols, and the biocatalytic applicability for structurally-defined substrates. The utilization of enzymatic co-factors in the synthesis and self-assembly of structures, as well as the role of naturally-sourced catalytic products, is another important area of thrust into the field (Ishida et al., 2010, Ding et al., 2011, Regueira et al., 2011, Weiz et al., 2011, Coyne et al., 2013, Scherlach and Hertweck, 2009, Biochemically engineered natural products (Lopez et al., 2007), metabolomics (Yuliana et al., 2011), enzymatic synthesis and its optimization studies (Ahmad et al., 2010), glycol bioengineering (Thibodeaux et al., 2007), substrate specificity bioengineering (Dunn and Khosla, 2013), and probes mechanism have recently been compared and contrasted for their functional efficacy

Natural Product Chemistry, Biosystematics, Physiology, and Biochemistry

Understanding the effects of biochemical interactions in physiological contexts on the generation of response-mediated phytochemicals, secondary metabolites, molecular templates, ion-clustered molecular systems, and ionic and non-ionic entities is vital. The generated clues within the biochemical set-up can help us understand the physiological effects on biogenesis, cellular signaling, and channels' functional roles for natural products entities of varying sizes and nature and other intended chemicals, with potential further applications in designing plants-based specific chemical's production in parallel with the microbial bio-engineering for metabolites production. Pathway breakthrough at different stages of natural and induced production of natural products in different biochemical and biogenetic settings might be understood through the bio-experimental release of the formed templates in the cellular systems and by finding an analogy with instances in the interdisciplinary sciences. This knowledge may find use in a variety of contexts, such as the study of drug-receptor and xenobiotic material interactions in vivo and in vitro. Inter and intra-molecular bio-chemical, physico-chemical interactions mechanisms (Nicolaou et al., 2004) of various chemo-biological entities in the natural biosystems, as well as cell-based signaling assays and their activator (McCulloch et al., 2009; Appendino et al., 2008; Pillon and Fogliani, 2009); bioactivity enhancements (Singh et al., 2015); More light can be shed on the natural products' participation in these fields if the steps in mechanistic pathways in physicochemical and biochemical proceedings with channel identification and usage (Marko, 2003, Mori, 1997) and their feedback in biomechanisms at functions are examined. They would, in turn, improve our knowledge of biogenesis, biosynthetic strategies, drug discovery probability, drug action, pharmacodynamics, adverse drug reactions, and synergism assessments.

Biological Origins, Biochemical Processes, Chemical Ecosystems, and Species Diversity

Symbiosis details on the structure and functions of the constituents are of utmost importance in the chemistry of natural products, as are the discoveries of biogenetic pathways of the biogenesis and production of designated compounds from marine and microbial sources (Xu et al., 2012, Dückert et al., 2012, Potowski et al., 2012, Suo, 1999, Weiz et al., 2014, Hennicke et al. Another facet of the interface between chemical ecology and natural products chemistry is the discovery of novel and aberrant biogenesis, the introduction of conceptual biosynthetic proposals, such as self-assembly and biosystems-based combinatorial methodologies (Newman et al., 2003a, Tulp and Solvay, 1999, Winter et al., 2011, Lin et al., 2013) with outcomes comparable to normal, ecologically elicited, and designed constituents (More focus has recently been placed on bioengineering natural product chemicals and comprehending their ecological interactions. The biogenetic agenda will focus on the effects of both exogenous and endogenous chemicals in the central and auxiliary pathways on the biogenesis of naturally produced constituents and the biocatalysis (Gatte-Picchi et al., 2014; He and Hertweck, 2003; Park et al., 2010). Natural products chemistry is expanding into new areas, such as chemical ecology, combinatorial chemistry, and retrosynthetic analysis, as well as total and semi-syntheses techniques and designs in organic chemistry approaches and developments of new routes and reactions (Roessner and Scott, 1996, Calixto et al., 2005, König et al., 2013, Sin et al., 2016).

Sustainable utilization of natural resources with broad green chemistry developments; the chemical nature of host-guest relationships and their applications in the production of natural products in the marine and amphibious environment; the toxicological behavior and toxicokinetics of natural toxins, toxic marine products, and other harmful plants, microbes, and fungi; and the chemical defense, symbiosis, and metabolic byproducts.

The role of its reactive and particular properties, as well as a more in-depth understanding of the steps of diverse biochemical processes (such as the effects of signal transduction within the chemical ecology domains and the precise roles of the natural signal regulators role in ecological interactions), can all contribute to the decoding of pathways.

Future concepts, foundations, and details in chemical ecology, plant evolution, biodiversity, chemiosmology, and pharmacognosy will be determined by the effects of acquired and evolved genome-derived patterns in guiding biochemical activities for species and their near and distant inter-relationships in the genomic tree in producing their molecular constituents.

From an Ecological, Environmental, and Chemical Viewpoint

The availability of authentic raw materials, the validity of herbal formulations, the outcome of chemical profiling, the quality of natural products, essential oils, and other plant-derived products, and the presence or absence of active mono- or poly-constituents in various natural sources have all been significantly affected by ecological and environmental changes, changes in geographical areas, phylogenetic cross-overs, and species purity. Artificial adulteration of natural resources and raw materials has spread to counterfeit herbal concoctions, which care nothing about the authenticity of their ingredients or the safety and efficacy of their intended use. Other factors, such as the up-reach of artificial chemical entities in the ecological system and ultimately to the end-product natural resources, including food chains, have also contributed to the depletion of these supplies. Sustainable resource protection, cultivation, and promotion of bio-diversity maintenance have all benefited from natural approaches to problem identification and treatment. Both chemists and biologists have recently begun to take an interest in the ecological consequence of their work. To better understand the biochemical and bio-mechanistic aspects of dealing with ecology in the future, we can use a template adapted from phyto, marine, and microbial chemistry (Larsen et al., 2005; Costello and Ward, 2006; Arnold and Targett, 2002; Garson, 2001).

Chemical Processes in Microbes, Oceans, and Light

Over the past fifty years, the antibiotic spectrum has been dominated by products of microbial chemistry (Genilloud, 2014). Beneficial metabolites have been created by the genus Streptomyces, although the same molecular framework compounds have been produced by Streptomyces from a wide variety of ecologically distinct sources. This immediately calls for a search for novel molecular templates that boast enhanced and varied biological features. Antibiotics, antimicrobials, antibacterials, antifungals, anticancer, and antimitotics, for example, may be derived from the anaerobic and uncommon actinobacteria found in mangrove habitats (Behnken and Hertweck, 2012; Paterson et al., 2009; Azman et al., 2015). The development of microbial metabolites as a source of new and frequently-resistance major known antibacterials for the concurrently-evolving super-resistant microbial species depends on the profiling of metabolic products (Larsen et al., 2005, Abdallah, 2011) and the roles of new and integrated interdisciplinary approaches for unmet clinical needs. Recent years have seen the publication of novel methods for the stereochemical structure determination of myxobacterial metabolites (Menche, 2008), the bioengineering of polyketides in fungi (Agarwal and Moore, 2010, Yin et al., 2013), dereplication through the use of spectro-analytical methods (Klitgaard et al., 2014, Nielsen and Larsen, 2015), and the interesting combinatorial biosynthesis of plant-specific products Natural product chemistry was fundamentally altered by breakthroughs in isolating, characterizing, and utilizing a wide range of biological activities from marine constituents. Novel molecular frameworks with diverse structural features have been discovered, expanding the pool of potential starting points for screening against important pharmacological classes. These developments also aided our comprehension of the symbiotic relationships that exist between marine animals. As the field progressed, researchers discovered the components of marine-dwelling fungi and another bacteria (Schmidt et al., 2005, Schmidt, 2005, Penesyan et al., 2010, Gundersen, 2013, Davis et al., 2012, Li et al., 2014, Lin et al., 2012, Uria and Piel., 2009).

More information about the sun's effects on plants, their products, and the nitty-gritty details of the chemistry being performed in the plant system can be gleaned from the natural products' reactivity and end-product variations of the photochemical setup, the phytotransformation diversity, and the final product(s) formation with regard to pathways selection and its alternate execution (Schümann and Hertweck, 2007, Nelson et al., 2007). It is possible that a new molecular framework for drug development could be provided by the new photo-product(s) from new, novel, and known substrates exposed to solar and non-solar sources. Recently published research on the photo behavior of curcumin in the zwitterionic micellar system (Banerjee et al., 2014) lends credence to this idea.

Analyses of Toxicity, Immuno modulation, and Kinetics

In ethnobotanical pharmacology, the protective and toxicity-ameliorating actions of naturally derived medicines are crucial. To confirm their safety and advance the creation of effective and safe medications, as well as better and superior-acting antidotes and antivenins, toxicological profiling of natural formulations utilized by the population is essential. The screening results for plants that protect against organ toxicity are widely reported (Lustosa et al., 2016). This is especially true for plants that protect against nephron and liver toxicity.

Toxicological effects and toxicokinetics of constituents, fractions, and plant parts, as well as toxicity by other naturally occurring raw sources from terrestrial and aquatic situations, can be better understood with reference to plants that produce severe toxicity (Ouédraogo et al., 2013; Tsuboy et al., 2010; Tu and Gaffield, 2000). Furthermore, the toxicological profiling, the extensive contamination in soil, air, and water with pollutions in the immediate surroundings of natural resources, with the necessary containment and chemical and biochemical remediation of the causes and amelioration of harmful products by the natural resources and natural products sources, may provide a deeper understanding and applications of chemical toxicology, inter-linked immunological broad-base, and natural products chemistry (L).

Functional and Crafted Meals

Leads for the agrochemical, neutraceutical, and food industries will be bolstered by the preparation and production of alternative and designer natural foodstuff and its formulations. This includes the development of super-nutritious foods, designer-food components and their procurement, purification, and formulations for selected nutritional value, and metabolic characteristics for a personalized prescription. There has been a recent focus on verifying the medicinal benefit of traditional foods and the bioactivity of dietary plants (Liu et al., 2016, FAO, 2011, Miroddi et al., 2013, Alfermann and Petersen, 1995, Luoma-aho, 2004, de Silva and Atal, 1995, Cseke et al., 2006).

Products of a Technical and Polymeric Nature

Biomedical sciences, biofuels, biomass availability, and as technical, industrial, and biomedical materials for environmentally friendly thrust in economies are all areas where scientists are constantly exploring new templates and honest answers to designer molecules like nanofibers, dendrimers, crown ethers, polymers, and natural gels (Anonymous, 2003; Tcheknavorian-Asenbauer, 1993).

From a phytochemical perspective, there is a need for more detail on the constituents, biological foundations, and bioactivity of agro-forestry-based phytochemicals, designer afforestation, and the development of genetically engineered renewable plant resources, genetic alterations in human foodstuffs, and genetic changes in microorganisms. The components of food, biomass, and bio-energy in the new millennium will be defined by their functions, the reactivity levels and the extent of activity of chemical products, and the environmental outreach via diverse biotic and abiotic mechanisms.

Data Mining and Computational Techniques

High-end technology developments in computational methods, data mining, and data management are required to keep up with the exponential growth of the plant sciences and natural products chemistry field. Better management of the informational repository, data mining, retrieval, as well as the safety, proper, benevolent, and beneficence of the envisioned leads, drug discovery and development, diversity in the broader natural products chemistry towards an understanding of the complete influence and impact on the interdisciplinary sciences, broader subject area's structural, functional, and various other applications in several domains, including medicine and veterinary medicine. New benchmarks for difficulties in bio-computing and computational resource management are being set as a result of the influence of chemical understandings in numerous interrelated sciences. Natural products chemistry and the contributions of natural products chemists have begun to have a significant impact. There is great hope for the future thanks to developments in computational methods and the prediction strategies and tools for the interactions between different types of natural resources in terms of their potential pathways, products, biomechanics properties, and software development (Lopez-Perez et al., 2007, Nakamura et al., 2014, Huang et al., 2007).

Effects on the Economy

From the perspective of natural products chemists and chemistry in general, the long- and short-term industrial, cultural, and economic impact is poised to take shape. Rouhi (2003), UNIDO (1991), Meinwald and Eisner (2001), Wagner (2004), Wijesekera (1991), Kingston (2011), de Silva (1997)a, and de Silva (1997)b all point to a growing interest in the industrial use of plant resources and their resulting technological impacts. The future of chemistry and related sciences and sub-disciplines in all of its branches and applications, as well as the broader economic scenario, will be profoundly impacted by natural product chemists' work in new methods and diversified fields (Harvey et al., 2015; Mullane et al., 2014).

CONCLUDING REMARKS AND DISCUSSION

Natural products as discovery scaffolds, comparative and co-products of biochemical settings and physiological conditions product outcome, designer food and its constituents, ecological and environmental probes compounds, and secondary-metabolite products of aberrant biogenesis, metabolic and marine products, revisions on ancient traditional herbal uses, and ethnobotany/ethnopharmacological understandings of underdeveloped regions have all contributed to reversing the unfavorable trend. We have benefited much from the use of natural products in industry, both as a source of a wide variety of technical grades and as a preferred method of economic benefits and as tools for scientific activity and biomedical applications, especially phytopharmaceuticals.

Natural products chemistry has had significant direct and indirect effects on the advancement of science and technology, playing key roles in both the development of new scientific understanding and the introduction of cuttingedge techniques and tools. Over the years, the economy has benefited greatly from the field's interconnectedness with the physicochemical sciences, medicine, and allied bio- and techno-industrial technologies. This was in addition to the benefits that the natural products industry already offered as a result of the use of indigenous technology, materials, and practices in resource collection and preparation.

Over a century after the first developments in chemistry, medicine, and technology, natural products and their chemistry appear to be playing an increasingly important role as a tool and a partner in the expanding interdisciplinary sciences, particularly in biology, biochemical and microbiological sciences, chemical ecology, in life sciences. Natural products chemistry is an emerging field with vast potential for advancing our understanding of biochemistry, ecology, and medicine. It will answer many questions we have about the natural world and present us with new ones to think about (Table 2).

Table 2 Some of the New Directions and Anticipated Outcomes for the Field of Natural Products Chemistry

Isolation, and Purification	Priorities for natural products isolation from contrasting bio-diversified areas, iden of traditional remedies' active constituents, search for new compound-templates
	Development of new techniques in identification & characterization of ligand-bo free substrates in plants,
	Fine separation methods and the need for finer, stable and chemically non techniques in isolation procedures, need for faster and efficient techniques to isc characterize larger molecules
	Purification and preservation of biological molecules' surroundings and asso chemical and physical during isolation
	Leading to safe, easily available and affordable plant-derived products; thrust and revival for natural products chemistry
Designer and Alien Molecules, Structure Elucidation	Versatile, and variable structures of new atomic compositions and elemental comb from marine and harsh terrestrial plants
	Natural answers to the designer molecules like carbon nanotube, fullerenes, crow etc., non-reactive fibers, natural gels for industrial use in food and non-food purpose fuel, plastics from plants, New techniques, and tools for structure elucidation spectro-analytical techniques
Drug Discovery, and Development	Currently ~50% of modern drugs of plant origin, share of synthetic drug steadily in over the previous decades, plant-based products in prophylactic role, perception of and zero toxicity driving push in phytochemicals as new chemical entity (NCE) development
	Small molecules drug discovery led to natural pool with plant pharmaceuticals and products reservoir from nature; new templates and designs based on nature
	Antibiotics and anti-cancers major class of plant-based drugs; prioritization, advan in strategy for newer techniques, and insight into the future drug discovery prov trends and impact on the phytopharmaceuticals worldwide
Bioactivity, Synergism, and HTS	Slowed and divided or partly ineffective biological activity, perceived ecolog environmental alterations, purity and originality of major product and constituents, of contaminations and man-made adulteration of the herbal products.
	Biological activity in single product *versus* multi-component products from pl synergy with no trace or watered-down activity of natural products, s metabolite *versus* the higher molecular weight non-polymeric/polymeric active component capable of receptor interactions, its identification as well as the expe replication of synergies associated in these single/multi-components
	High-throughput screening in purified natural products for template selection screening of natural products as crude extracts holds promise
Biomechanics	The discovery of new pathways in biosynthesis, novel conceptual biogenetic p including in self-assembly and combinatorial methodologies and its compatib comparability to other natural pathways
	Use of large and small enzymes and enzyme-mimetic templates in applicable phytochemistry and studies into the structural and physicochemical property chang enzyme and changes in the functional stage substrate, structures, behavior/resp biochemical properties
	Spectrum of biochemical processes- including signal transduction and structures c signal regulators and their electrochemical properties, all at first in smaller system

Thus, once more, the emerging trends and future promise from these advancements, and a deeper understanding of the natural products chemistry domains, with its interrelationship with natural and biological sciences and with the hereto hidden concepts/understandings in biotechnology, drug discovery, pharmaceutical sciences, genetics, and chemical ecology will help to race ahead and set the agenda for further work with the promise of new economic, and technical growth s. With the potential for discovering newer phytochemically-templated foodstuff, drugs, and all chemically viable items in an era of economic turndown, the current scenario of the developing fronts in the chemical, biochemical, and chemical ecology fields, as well as the commercial side of the research and developments, holds enormous promise and importance on a global scale. Focus and importance are growing on the field of natural products chemistry and the contributions of natural products chemists as a result of advances in science, technology, and economic turnarounds.

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