© JUN 2025 | IRE Journals | Volume 8 Issue 12 | ISSN: 2456-8880
DOI: https://doi.org/10.64388/IREV8I12-1723042

Design and Synthesis of Next-Generation Organic Therapeutics Using Molecular Engineering, Computational Drug Discovery, and Precision Medicinal Chemistry

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Abstract- ***The next generation of organic medicines is one great step forward in modern medicine, in which molecule engineering, in silico drug discovery, organic synthesis, and precision medicinal chemistry principles are merged to overcome the shortcomings of conventional drug development, in which small organic molecules such as heterocyclic compounds, natural product-based molecules, peptide mimics, and specific small-molecule drugs still dominate the discovery, and a plethora of therapies for treatment for difficult diseases, including cancer, infection, neurology, metabolic disease, inflammation diseases, and so on. However, conventional drug discovery is usually associated with longer discovery process, expensive expenditure and experiments, lower predictive efficacy for biological behavior, poor selectivities and resistances and possible adverse effects of drugs so it's necessary to explore rational ways to discover therapeutic molecules, on the contrary the higher complexity of biological target: protein, enzymes, signal pathways and molecular networks demands more intelligent way to generate better molecules, especially for drug-likeness. This framework puts forward an ideal plan, which combines molecule design and engineering, further organic synthesis strategies, computer-aided design of drug discovery (CADD) methods, including molecule docking, QSAR, and AI and its application in prediction of molecule activity, target prediction etc, based on the concept of precision medicine in drug discovery system. The approach from molecule engineering is based on modulation of molecule scaffold, functional group, and molecule-target interactions to tailor the desired characteristics including potency, stability, soluble and selectivity. CADD methodologies (ligand-target interactions, pharmacological properties, drug-likeness and potential toxicity estimation), followed by prediction system which can accelerate the entire process for better lead candidate selection, has enabled rational and rapid design of therapeutically active and effective agents, with increasing utilization of AI (including machine learning and deep learning) as well, to perform the high-throughput virtual screening. Combining these techniques helps us build an all-in-one drug discovery and development framework.***

Keywords: Medicinal chemistry, Organic therapeutics, Molecular engineering, Drug discovery, Computational chemistry, Molecular docking

I. INTRODUCTION AND BACKGROUND RELATED TO THE STUDY

Organic therapeutics are one of the cornerstone disciplines of modern medicine; organic molecules which are structurally diverse may interact in a selective fashion with targets within the body, modulate signaling pathways responsible for pathological states and may ultimately be designed for successful treatment of a multitude of diseases in the human population where there has historically been considerable success with the development of small-molecule drugs as this enabled pharmacological intervention into complex conditions such as cancers, infectious, neurologic and cardiovascular diseases and endocrine or metabolic problems; small molecules remain a focal point in drug discovery because of their ability to be chemically altered through various molecular engineering strategies to increase potency, improve selectivity, alter pharmacological performance, or increase the drug safety profile; as a drug modality within oncology, organic molecules have been a pivotal factor through the development of cytotoxic agents, targeting molecules of disease and also hormone-based and custom-designed molecular drugs that function to disrupt a series of critical physiological processes such as DNA replication and division and neovascularization or signaling pathways, with specific example of kinase inhibitors,

DNA-interacting molecules based on heterocyclic organic scaffolds and apotosis-inducing compounds having enhanced prognosis for patients with various malignancies and medicinal chemistry has continued to provide highly selective agents designed to target specific proteins such as receptors for tyrosine kinases so avoiding damaging effects that occur as a result of standard therapy such as that associated with cytotoxic chemotherapy (Varmus, 2016); in development against microbial infection, organic molecules including beta-lactam antibiotics, quinolone derivatives, sulphonamides, triazoles and diverse heterocyclic compounds have offered successful treatments for infectious problems resulting from bacterium, fungus or parasite organisms through mechanisms that affect bacterial cell wall construction, synthesis of nucleic acid and target enzyme pathways but an increasing incidence of resistance amongst microbes has presented continued challenge creating ongoing need for molecular novelty or alternative treatment regimes. With regard to neurology there has been huge progress with development of organic compounds effective in diseases of the central nervous system through effects on neurotransmitters, channels, receptors, enzymes; of clinical utility in patients with Alzheimer's, Parkinson's and epilepsy, depression or anxieties respectively; molecular modification in these diseases remains a key aspect of improving patient treatment not only for increased specificity but in consideration of blood-brain barrier permeation and the potential effects upon safety. Cardiovascular medicine has been fundamentally revolutionized by organic therapeutics; use of statins to modulate lipid levels, anticoagulants in managing clotting cascades, antihypertensives and calcium channel blockers affecting pressure and vascular tone as well as antagonists or activators for receptors in controlling circulation have all been widely adopted treatment strategies which directly lower risk and improved cardiac care, whilst in metabolic disease development such as diabetes, obesity or various endocrine disorders, targeted agents such as inhibitors, receptor agonists or antagonists hormone mimics have been designed to affect various metabolic pathways, again becoming ever more specific, or in the treatment of hyperglycaemia: nevertheless, there has been an identified need for next generation approaches to this drug design field through improved molecular engineering of targets, accounting for patient population variation and drug resistance, and consideration of toxicity profiles through combination computational and experimental drug discovery with artificial intelligence approaches in medicinally targeted fields in the next era of medicine; consequently organic molecule remain a cornerstone drug discovery platform which are, together with these new techniques involving synthetic chemistry, computer analysis, predictive modeling combined with an assessment of their biology, enabling advancement in therapeutic drug discovery of potent selective safe human treatments.

II. HISTORICAL DEVELOPMENT OF ORGANIC THERAPEUTICS

Organic therapeutics have evolved historically and continue to be discovered and developed more and more toward highly engineered, computer-designed and personalized therapeutic molecules, for the earlier discoveries of therapeutics relied more heavily on naturally occurring medicinal substances isolated from plants, microbes and many other sources as these provided with many varied and complex molecular structures possessing strong biological effects, alkaloids and terpenoids and antibiotic substances as examples that are all derived from nature thus formed the backbone of the modern pharmacology with demonstrating that certain highly intricate natural structures are capable of binding with high selectivity to physiological targets; typical drugs obtained from natural sources included in the list of major discoveries are alkaloid derived medicines of morphine’s and quiines, terpenoid derived anticancer medicines of paclitaxel, microbial derived antibiotics that revolutionized the treatment of bacterial, fungal or other infections as that stated in one of my own projects previously; from the complex natural structures aforementioned above, valuable chemical scaffolding was indeed derived, on which a further series of medicinal optimization took place and subsequently was used as a starting point. Thus, along with the development of synthetic medicinal chemistry era where chemical synthesis allowed systematic drug designing and optimization of organic compounds leading to the identification of a series of heterocycles drugs, small molecule inhibitors and target specific agents that possessed improved pharmacophore, heterocycles like nitrogen, oxygen

and sulfur based cyclic compounds were preferred given that their electronic structures can tune various crucial characteristics such as binding affinity to target receptors, solubility, metabolic stability and efficacy on targeting molecules and signaling proteins (Swinney, 2013) to modulate specific target activity or signaling pathway(s) involved in pathological processes while small molecule inhibitors offered very specific ways to modulate pathological conditions through target related activities of enzymes, receptors and other molecules. Furthermore, with the increase in identification of biological target(s) of biological macromolecules related to medical conditions, a paradigm shift in pharmaceutical research, from traditional phenotypic screening toward rationally-defined target-based research has been initiated and consequently medicinal chemistry had integrated structural biology, computation chemistry and pharmacology in conjunction (Swinney, 2013) as to rational designing of therapeutic molecules; currently, driven by individual biological makeups and with identification of individual biomarkers/medical conditions of individuals being targeted, precision medicine approach offers further revolution to integrate genes, medical diagnostics/biomarkers of individuals and molecular profiling toward design of more selective, potent, safe, well-tolerated and more efficient therapies that are specifically prescribed to an individual. Especially biomarker directed drug therapies which specifically target pathways dependent on some biological phenomena at cell level have resulted in efficient treatments of targeted malignant diseases. Combined with genetic features of each individual/medical conditions, molecular profiling/biomarkers and computational prediction for efficacy of particular drug, personalized medicine therapy further enhanced efficient prescription to maximize and optimize drug treatment response and improve tolerance toward the drugs.

III. ORGANIC SYNTHESIS APPROACHES

The development of next-generation organic therapeutics depends strongly on efficient synthetic strategies capable of constructing structurally diverse molecules with optimized biological properties, where classical organic reactions have historically provided the fundamental methodologies for preparing pharmaceutical compounds and biologically active molecules through controlled formation of carbon–carbon and carbon–heteroatom bonds; traditional synthetic approaches such as alkylation reactions enable introduction of alkyl groups into molecular frameworks by forming new carbon–carbon or carbon–heteroatom linkages, thereby allowing modification of molecular size, polarity, and biological activity, while acylation reactions provide important pathways for incorporating carbonyl-containing functional groups that influence molecular recognition, stability, and pharmacological behaviour; condensation reactions represent another essential synthetic strategy because they facilitate formation of complex structures through elimination processes, enabling preparation of imines, amides, heterocycles, and other therapeutically relevant molecular architectures, whereas cyclization reactions allow construction of cyclic and fused-ring systems that are frequently found in bioactive compounds, including heterocyclic scaffolds widely used in medicinal chemistry; however, increasing demands for environmentally responsible and efficient drug discovery have encouraged development of modern synthetic methodologies that overcome limitations associated with conventional multi-step procedures, excessive waste generation, and harsh reaction conditions; click chemistry has emerged as a powerful approach for rapidly assembling molecules through highly selective, modular, and efficient transformations, with applications in drug discovery, chemical biology, and molecular imaging (Kolb et al., 2001); green synthesis strategies further emphasize reduction of hazardous reagents, improved atom economy, safer solvents, renewable resources, and energy-efficient processes to support sustainable pharmaceutical manufacturing (Anastas & Warner, 1998); photocatalytic synthesis has expanded organic reaction capabilities by utilizing light energy to generate reactive intermediates under mild conditions, enabling selective bond formation, radical transformations, and late-stage functionalization of complex molecules; similarly, biocatalysis employs enzymes and engineered biological catalysts to achieve highly selective transformations with excellent stereo control, mild operating conditions, and reduced environmental impact; therefore, the integration of classical organic reactions with advanced methodologies such as click chemistry, green synthesis, photocatalysis, and biocatalysis

provides a comprehensive synthetic framework for designing and producing next-generation therapeutic molecules with improved efficacy, selectivity, sustainability, and pharmaceutical relevance.

IV. BIOLOGICAL EVALUATION STRATEGY

Biological evaluation of the new generation organic therapeutics constitutes a fundamental and indispensable part of drug discovery since it sets a balance between molecular structure, biological activity and therapeutic action. Newly synthesized organic molecules require to be systematically evaluated using cellular, biochemical and molecular tools that determine their effectiveness, specificity and safety profiles. In research focused on anticancer agents, the most often used in vitro method for the biological assessment is, among others, the MTT assay, which quantifies living cells metabolic activity through reduction by viable cells of the colored tetrazolium salt tetrazolium salt to formazan and gives information relative to compound's cytotoxic effect and inhibition of tumor cell proliferation. In addition, cell viability studies assess concentration-dependent responses, effects of growth inhibition as well as selectivity between malignant and non-malignant cells and further investigation about mechanisms of programmed death (apoptosis) can reveal whether target compounds operate via this process through morphological changes, mitochondria dysfunction, damage to DNA, activation of caspase effectors or components of apoptosis signaling pathways (Galluzzi et al., 2018). Antimicrobial evaluation serves for analysis of organic molecules having potential anti-infective activities and it is usually based on microdilution method for determining minimum inhibitory concentrations (MICs), where the lowest concentration that prevents visible microbial growth is measured and a useful value relative to potency (antibacterial or antifungal) of the agent is obtained and it is often completed by determination of inhibition of growth curves, reflecting the ability of compounds to repress microbial growth. Although phenotypic assays reflect the overall outcome of compound treatment, studies of the molecular mechanism of action of therapeutics is crucial and usually takes place by determining interactions of studied molecules with targets by methods as enzyme inhibition assay where influence of drugs on disease related enzyme activity is revealed, protein-drug interaction determination by the use of various biophysical techniques or by the examination of effects of compounds on specific signaling pathways through their impact on protein kinase activity or signaling events. Molecular approaches as well as cell imaging assays, such as molecular docking, proteomic analysis of differential expressed proteins or genes expression study are capable of further correlating molecule interactions with observed effects. Hence, the use of cell cultures assays, microbial activity evaluation, biochemical examination of proteins and examination of mechanism of action via various cellular and biochemical methods would provide a detailed description to confirm therapeutic possibilities of any new compound.

V. DISCUSSION

Next-generation organic therapeutics is predicted to lead in significant gains in performance, selectivity and safety. Rationally developed molecular engineering, computational drug design and precise medicinal chemistry should combine molecular design with prediction tools. Improved therapeutic activity will result from optimizing molecular structure by targeting specific parts of chemical scaffolds, functional and chiral features and physiochemical features. Target specific molecular design permits the identification and optimization of molecules, which preferentially activate or inhibit those disease-specific protein, enzymes, receptor or signaling pathways of the body so as to enhance therapeutic activity with an avoidance of unwanted and toxic effects. Computer prediction models can inform such activities as target-ligand interactions, binding affinity of them and the stability and biological activity of the potential compounds and may inform molecular dynamics, QSAR prediction, and docking analyses using molecular visualization software and AI for determining how these types of parameters influence them with prior extensive evaluation through computational and modeling simulations (Sliwoski, D; Ma, L; (9), W. N) (2014); the enhanced selectivity is achieved by structural modulative strategies including molecular scaffold, bioisosteric displacement, substituent modifications, and pharmacophore, to guide lead molecule targeting desired receptors and inhibiting unwanted interactions, leading to

optimization of structure with reduced off-target side effects, lowering the risk of failures; toxicity and unfavorable side effects is greatly reduced due to the combined effects of absorption distribution metabolism excretes and toxicity(ADMET) prediction models with high-throughput virtual screening technologies when testing and predicting the molecule with high risks and issues such as drug metabolism and undesirable pharmacology behavior in early research and evaluation stages and failure rates at clinical trial stages of future research (Vamathevan J; Antony S, Z.)(2019); AI powered techniques together with large chemical libraries are used to identify molecules with desirable profile using screening platforms to evaluate numerous compound designs, and predict their behavior as well. Thus, rational molecule optimization, target-selective molecular design, computer prediction, structural adjustment, ADMET prediction along with AI-powered high-throughput screening has furnished the platform on behalf of precise drug design towards future and present therapeutic approaches against many illnesses more precisely with favorable safety, selectivity and highest activity of organic candidates developed by human body for future generation therapeutics.

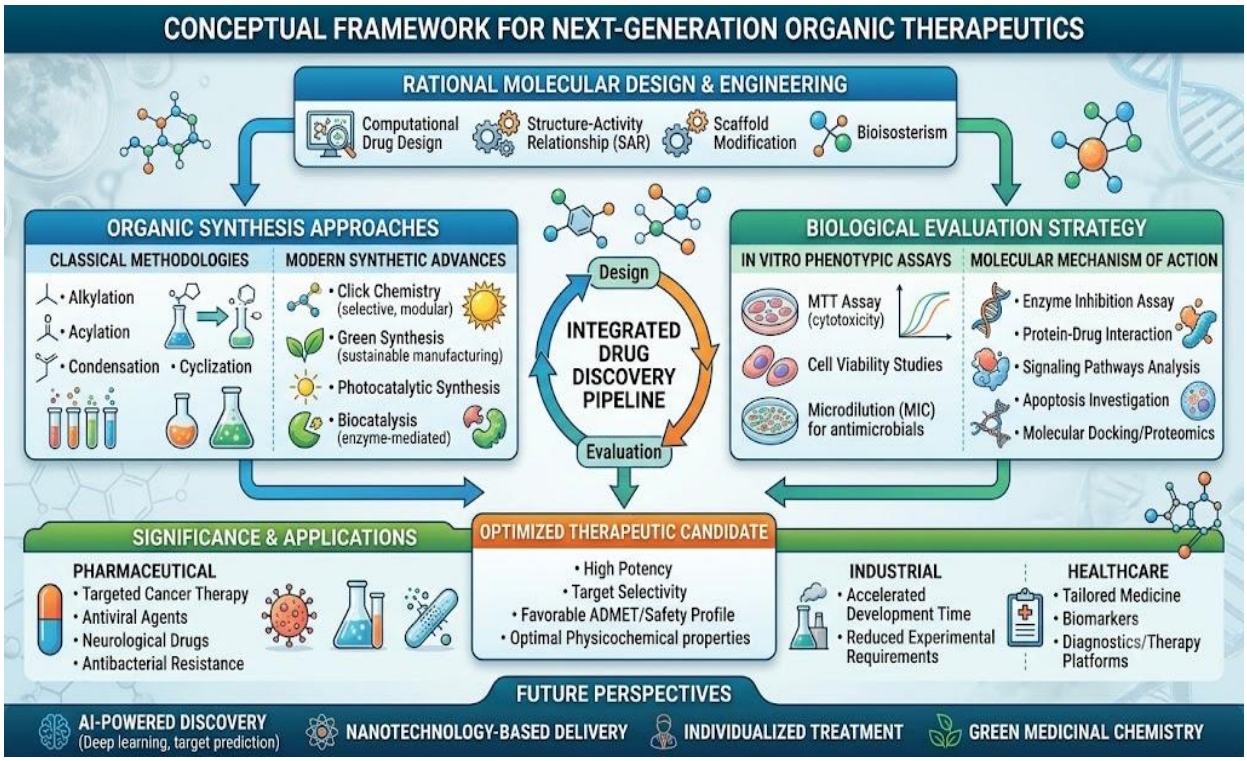
VI. APPLICATIONS RELATED THE STUDY

Next-generation organic therapeutics through molecular engineering, computational drug discovery and precision medicinal chemistry offer substantial promise for the progress of health care since it can enable the design of exquisitely specific, biologically active, and pharmacologically optimized therapeutic molecules that would overcome myriad complex medical challenges, and one of the most important aspects of this is the pharmaceutical application of molecularly engineered organic compounds since organic molecules remain the central building blocks for various drugs including those for cancer therapy, anti-virus agent, and treatments for disease of the nervous system or neurological illness; for cancer patients, organic molecules (kinose inhibitors, apoptosis regulator, etc) designed through molecular engineering target tumor-specific pathological process to improve the therapy efficiency and drugs designed with the aide of computation approaches achieve better therapeutic potency with lower toxicity; and for viral diseases, rationally designed organic compounds that can target the structure of a vital component of a virus (like viral enzyme), a process that a virus performs in order to replicate itself or interactions between host cells and the virus are helpful to inhibit the spread and infection rate with the help of computational approach; organic synthesis research remains a cornerstone for developing novel antibacterial drug agents to combat with microbial resistances through improved target engagement and biological recognition: and to the area of neurogenic diseases, organic molecules with optimum functional groups, structure or three-dimensional arrangement are designed to improve receptor modulation, enzyme inhibition, and neurotransmitter receptors/ion channels function and neurotransmitters pathway signaling in neurological diseases (like Alzheimer's disease, Parkinson's disease, epilepsy, or depression); However, challenges of blood brain barrier and long-term use with side effect necessitate the superior drug designing strategies in neurogenic drugs; furthermore, by combining genomic technologies, molecular characterization and bio-markers determination, patient-personalized therapies were established based on the integration of individual molecular profiling and diseases state enabling targeted molecule based individual therapy; this type of personalized molecular targeted drugs are particularly useful for cancer and rare diseases treatment; Additionally, application of biotechnology becomes much more integrated in diagnosis devices and therapeutic systems as the progress of organic synthesis combined with computation prediction and biological investigation in development of molecular diagnostics and therapy platform. Molecular probes, imaging reagents and molecular recognition elements will act as effective biological detection device or indicators while delivery system integrated with small molecules become more prevalent. The combination of molecular engineering, artificial intelligent mediated drug discovering and precision medicinal chemistry thus form a systematic paradigm that encompasses novel pharmaceutical, patient-personalized therapy, sophisticated diagnosis tools as well as robust bio-tech platform that aims to fulfill the requirements in solving health problems.

VII. SIGNIFICANCE OF THE STUDY

The current conceptual study has remarkable scientific, pharmaceutic, industrial, and healthcare importance by constructing a convergent framework integrating medicinal chemistry, molecular engineering, computational drug discovery and designing a precise therapeutics based for modern organic therapeutics-with the scientific importance resting in that an enhanced comprehension of structural features of molecules, functionalities of chemistries, biological activities and mechanisms of pharmacological effects will permit the researchers of tomorrow more readily optimize structure for enhanced drug efficacy, and in which computer simulation approaches, molecular docking, Quantitative Structure-Activity Relationship (QSAR) analysis, Artificial Intelligent (AI)-based predication strategies along with innovative synthetics routes present the advantage of enabling rational molecular designs to be put into practice as computational data could be readily interpreted, to obtain predicting of biological activities and optimizing leads and exploring Structure-Activity Relationship (SAR) more effectively than random traditional empirical ones (Sliwoski et al., 2014)-and thus adds to our knowledge in relation to designing better organic drugs in terms of modifying scaffold structures, optimisation of functional group elements and identifying substitution sites, utilizing bioisosteric transformations, and developing molecules targeted against certain biomedical targets, which ultimately enhance the potency, selectivity and all aspects related to pharmacological activity of chemical entities, whilst its significance in a pharmaceutic level means that this proposed methodology can reduce unfavorable side effects that might originate from unwanted off-target interactions and improve a drug's likeness of a medicine in a form that enables the detection of potential absorption, distribution, metabolism, excretion, and toxicity (ADMET) early in the drug discovery program by increasing the success rate of further developments (Vamathevan et al., 2019). Industrially, combining computational power, auto devices with precision chemistry can indeed accelerate pharmaceutic development pipeline time, reduce unnecessary experimental requirements and thus save valuable scientific resource time required to identify effective drug lead; and for a healthcare perspective the framework proposed supports tailored medicine since selection of suitable therapeutic agents could be based on their molecular structure, individual patients being characterized by biomarkers and tailored regimes being provided for individual cases especially with complex diseases where human biological variation could affect the response of a therapy. Overall, the unification of organic synthesis and computational wisdom to develop precisely targeted medications with heightened effectivity, decreased potential side effects and increased therapeutic usefulness could facilitate new achievements in pharmaceutic investigation.

© JUN 2025 | IRE Journals | Volume 8 Issue 12 | ISSN: 2456-8880
DOI: https://doi.org/10.64388/IREV8I12-1723042



Above diagram showing Design and Synthesis of Next-Generation Organic Therapeutics

VIII. FUTURE PERSPECTIVES

The future development of next-generation organic therapeutics is expected to be strongly influenced by the integration of artificial intelligence-assisted drug discovery, nanotechnology-based delivery platforms, personalized therapeutic strategies, and green medicinal chemistry approaches, where artificial intelligence provides transformative opportunities for accelerating pharmaceutical innovation through molecular generation, target prediction, and computational optimization of therapeutic candidates; AI-driven generative models, machine learning algorithms, and deep learning frameworks can analyse large-scale chemical and biological datasets to design novel molecular structures, predict drug–target interactions, optimize pharmacological properties, and identify promising lead compounds with improved activity and safety profiles, thereby reducing dependence on extensive experimental screening and accelerating early-stage drug discovery processes (Vamathevan et al., 2019); target prediction approaches further enable identification of disease-associated proteins, biological pathways, and molecular mechanisms, supporting development of more selective therapeutic molecules through precision-oriented design strategies; nanotechnology-based delivery systems represent another important future direction by improving the transport, stability, bioavailability, and targeted distribution of therapeutic compounds, where nanocarriers including liposomes, polymeric nanoparticles, lipid nanoparticles, and inorganic nanostructures provide controlled delivery platforms capable of enhancing drug accumulation at specific biological sites while reducing systemic toxicity; targeted delivery approaches combining molecular recognition elements, surface modification strategies, and responsive nanomaterials offer potential solutions for improving therapeutic efficiency in complex diseases; personalized therapeutics are also expected to expand through integration of genomic analysis, biomarker identification, molecular diagnostics, and computational patient profiling, particularly in precision oncology where tumor-specific molecular alterations guide selection of targeted drugs and individualized treatment strategies; furthermore, green medicinal chemistry will play an essential role in future pharmaceutical manufacturing by promoting sustainable synthetic methods, improved atom

economy, reduced chemical waste, renewable resources, energy-efficient transformations, and safer solvent systems, thereby minimizing environmental impact associated with drug production (Sheldon, 2017); therefore, the convergence of artificial intelligence, nanotechnology, precision medicine, and sustainable chemistry provides a comprehensive future framework for developing highly effective, safer, environmentally responsible, and patient-centred organic therapeutics.

IX. CONCLUSION

The utilization of molecular engineering integrated with computational drug design, sophisticated organic synthesis and precise medicinal chemistry provides an optimistic direction toward a more intelligent, efficient and personalized approach of discovery of the novel organic therapeutics of new generation; Molecular engineering allows it to be employed as a foundational approach in the design of therapeutic agents as it aids in the systematic modification of chemical scaffold, functionality, stereochemistry and the interaction of molecules that enhance their activities toward specific biologic targets, selectivity, stability, pharmacologic performance, etc. While applying to studies of structure-activity relationship, bioisosteric modifications, and target directed molecular designs, it provides us with better candidate compounds than the traditional discovery strategies, those have improved efficacy with potentially lower undesired activities. Computational approaches allow us to save time, money and other resources by reducing lengthy and time-consuming experimental works via virtual screening, docking, molecular dynamics simulations, QSAR models, AI based methods...; Moreover, combined application of AI, automated synthesis and precise medicinal approaches established the foundation for the novel drug development system based on predicative molecule design and patient specific treatment strategies-such as personalized medicinal prescriptions based on biomarkers etc; AI based techniques can efficiently analyze complex chemical/biological databases and predict drug candidates efficacy, toxicity, as well as optimum synthetic pathway, organic synthesis will make that complex molecules practically available in good functional properties; Thus, combined efforts can create highly selective, effective and safety therapeutic agents for use in pharmaceutical researches and biotechnology which may benefit personalized medicine and efficient drug development system to more extent.

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