Current Advances in Drug Design and Cancer Research

This editorial provides a brief overview of the thematic issue and the papers. Modern manufacturing has become efficient and cheap with the development of technologies. However, this technological leap has not been reflected in drug design. The success rate of new drug development is quite low from its first phase to the final approval. Cancer is one of the most enduring challenges for human beings. Various methods are being researched to prevent, control, and cure cancer. However, there is still a long way to go before reaching the ultimate goal. This thematic issue is proposed to help biologists and physicians track the current advances in drug design and cancer research. The collection of the thematic issue includes five reviews and two research articles. The first review explores various COVID-19 targets and quests the corresponding inhibitors. The second one focuses on surveying the latest research related to the public database and computation-based predictors of anti-cancer peptides. The third one reports the relevance of aromatase inhibitors in breast cancer treatment. The fourth review discusses the advancement in nanotechnology and its applications for cancer treatment and diagnostics. The fifth one collects the latest research about 1,3,4-Oxadiazoles as potential pharmacophores for cytotoxic potentiality. The sixth research isolates myricanol-9-acetate and myricanol from the ethyl acetate extract of the bark of the plant and evaluates them for anti-cancer activity. The last research reports the synthesis of amido-derivatives of silybin, hydnocarpin D, and isosilandrin and a preliminary evaluation of their cytotoxicity against cancer cell activity.

Despite the increase of advanced technologies applied in developing new drugs, the launch of a successful drug is still time-consuming, labor-intensive, and risk-uncontrollable [1-3]. In general, the phases for new drugs include target/lead development, preclinical trials, clinical trials, authority review (e.g., Food and Drug Administration in the USA and European Medicines Agency in Europe), and post-approval safety monitoring. Efficient development of the first three phases promises a high probability of success for the rest of the stages [4, 5]. The first stage of modern drug discovery involves target identification, hit discovery, lead identification, and candidate optimization [6]. After that, preclinical trials test the new drug on non-human subjects to determine the efficacy and safety, which provides useful clues for clinical trials [7]. However, the drug and vaccine for COVID-19 is a different story. The huge impact of the pandemic motivates researchers in different fields all over the world to accelerate the progress of drug design and vaccine development [8]. The potential vaccines get into the third phase, i.e., clinical trials, in only 6 months after obtaining the sequencing results from patients [9]. This is almost four times faster than the development of a normal vaccine in the past.

In contrast to the short-term impact of the COVID-19, cancer is long challenging and constitutes a major threat to public health [10]. It usually causes fatal and irreversible impairments in the human body. A recent survey from the World Health Organization (WHO) shows that about 18 million new cancer cases were diagnosed in 2019 [11]. WHO also warns that if current trends continue, the world will see a 60% increase in cancer cases over the next 20 years. Cancer results from abnormal proliferation of various types of cells in the body. Diagnosis and control of cancer at the earliest possible stage provides the best chance for successful treatments [12]. Effective cancer treatments include chemotherapy [13], radiation therapy [14], stem cell transplant [15], immunotherapy [16], targeted therapy [17], surgery [18], etc.

With these perspectives, this thematic issue focuses on summarizing the latest literature and pointing future directions in drug design and cancer research. Now, we turn to the content of this thematic issue, which contains five reviews and two research articles. The first review explores various COVID-19 targets and quest for the corresponding inhibitors. In 2020, the unprecedented COVID-19 profoundly and permanently changed the world [10]. At this moment (March 2021), it is still endangering human lives worldwide, presenting an unprecedented challenge to public health, food systems, social order, and almost every aspect of the world [19]. The author claims that the COVID-19 chemotherapeutics have to be designed to inhibit this quorum-sensing mechanism to destroy the drug resistance. The spike proteins of CoV binds to the cellular receptor ACE 2, followed by the entry of the viral RNA genome. The drugs which are used against COPD, dyspnoea, severe pneumonia, and pulmonary lesions could be reused to combat COVID-19. Currently, researchers are still unable to confirm the sequelae of COVID-19 treatment and the side effects of the related vaccines. For complete recovery, there is a need for deep and elaborate studies on genomic sequences and invading mechanisms in the host cell.

The second review summarizes the latest computation-based research of anti-cancer peptides. Compared with conventional treatments, which include chemotherapy, radiation therapy, and stem cell transplant, peptide-based therapy is becoming more favourable since it is featured by high target specificity, low toxicity, and is easily synthesized [20]. In clinical practice, peptide-based therapy is usually employed as adjuvant intervention together with other types of treatments [21, 22]. The main contents of this review include publicly available databases of anti-cancer peptides, benchmark datasets, feature construction, feature selection, machine learning algorithms, evaluation methods, performance measures, performance comparison of different methods on a benchmark dataset, and currently available webservers/software. In this review, the authors discuss future perspectives in investigating the anti-cancer peptides. Besides that, they also prompt several recommendations that can be considered to further improve the quality of the anti-cancer peptides and the performance of potential novel approaches.
The third article reports the relevance of aromatase inhibitors in breast cancer treatment. Aromatase is defined as a cytochrome P450 enzyme complex, which has been proved to be responsible for the conversion of androgens to estrogens [23]. In breast cancer, aromatase is expressed in tumoral stromal cells, adipose, and epithelial cells adjoining the carcinoma [24]. This study states particulars about the currently approved steroidal and non-steroidal aromatase inhibitors for clinical use and the adverse effects. A combination of aromatase inhibitors along with some COX-2 inhibitors may enhance efficacy. This review provides researchers with vast and absolute knowledge about aromatase inhibitors and uses this knowledge for the study and synthesis of more potent, efficacious, and safer compounds in the future.

The subject of the fourth review deals with nanotechnology, which is expected to be a promising tool for diagnostics and treatment of cancer. Cancer has become one of the major public health concerns with the second leading cause of death. Conventional cancer therapy methods have side effects, and diagnostics techniques are time-consuming and expensive. Nanotechnology has improved the controlled drug delivery due to its beneficial nano-size along with betterment in the treatment, diagnosis, and prevention of various diseases [25, 26]. It has been used as biosensors and as an advanced and effective treatment in the medical field. In this review paper, the authors also discuss the advancement in nanotechnology and its applications for cancer treatment and diagnostics and highlight challenges for translation of these advanced nano-based techniques for clinical applications and their green synthesis.

The fifth review collects the latest research about 1,3,4-Oxadiazoles as potential pharmacophores for cytotoxic potentiality. Oxadiazole shows a wide range of pharmacological activities, and it is frequently used in medicinal chemistry [27, 28]. The authors survey related literature and demonstrate that 1,3,4 oxadiazole is an excellent moiety with a lot of pharmacological activities. This moiety has shown specific potential against cancer. 1,3,4 oxadiazole and its derivatives have inhibitory properties against the receptors or enzymes which are responsible for cancer. The use of 1,3,4 oxadiazole against cancer is expected to be a brilliant moiety and has a large scope for interest for the researchers.

We shall turn to the two research articles, which conduct a thorough investigation into Myricanol-9-acetate and Silybin/Hydnocarpin D/Silandrin, respectively. Myricanol-9-acetate is a naturally existing derivative of myricanol reported from the plant [29]. The authors isolated myricanol-9-acetate and myricanol from the ethyl acetate extract of the bark of the plant and evaluated them for anti-cancer activity. Their study demonstrated the potential of MA to serve as an important candidate in the development of anti-cancer agents, and it provides a high scope for proceeding to animal and preclinical studies. The molecule is expected to be devoid of toxicity as M. esculenta is used in the traditional system of medicine and as a nutraceutical.

The last research article involves the investigation of silybin to derivatives of hydnocarpin D and isosilandrin. The authors achieved the chemical transformation of silybin to derivatives of hydnocarpin D and isosilandrin and then evaluated cytotoxicity of these derivatives against human non-small cell lung cancer cells (A549), human breast cancer cells (MCF-7), and cervical cancer cells (HeLa). This study synthesized 45 new amido-derivatives. They also empirically proved that some of these amido-derivatives showed moderate to good antiproliferative potency against cancer cells. The empirically compound 10j was further testified by colony formation assay and molecular docking.

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