Recent Developments in the Medicinal Chemistry for New Small-Molecule Therapeutics to Treat HIV-AIDS

In early 1981 a new disease epidemic was reported by the CDC (Centers for Disease Control and Prevention) [1] which was later termed as AIDS (Acquired Immunodeficiency Syndrome) and subsequently, it was identified that the disease is caused by the retrovirus HIV (Human Immunodeficiency Virus) [2]. Since then, scientists from all over the world joined forces to find an effective treatment for the disease and in 1987 the first anti-HIV drug called AZT (azidothymidine) or zidovudine was approved by U.S. FDA (Food and Drug Administration). Within 10 years of discovery of the first antiretroviral drug, the most effective treatment for AIDS was developed, a multidrug combination therapy, widely known as HAART (highly active antiretroviral therapy) or cART (combination antiretroviral therapy) [3]. More than 30 drugs have been invented until now and are being used in different combinations depending on patient response to treatment [4]. Although, the decline of HIV related deaths from a peak of 1.9 million [1.4 million–2.7 million] in 2004 to 940,000 [670,000-1.3 million] in 2017 was achieved through the use of HAART, there are still limitations associated with this treatment such as viral resistance to drugs, toxicity and adverse side effects of drug use and long term drug compliance [5]. Therefore, to overcome all these complexities of antiretroviral treatment, novel drug development with intense clinical study is required. In this thematic issue, the advancement of antiretroviral therapy over the years, their limitations and development of novel drug formulations or regimen to address the limitations has been outlined in details.

Antiretroviral therapy (ART) is the HIV medication that reduces the overall viral load and suppresses the probability of acquiring opportunistic infection. ART is not a cure for HIV infected patients, but it increases the life expectancy of patients to facilitate their healthy survival. ART has different combinations of drugs and Protease inhibitor is one of the important constituents among them. Protease inhibitor impedes the HIV-1 aspartyl protease and blocks mature virion formation. In the review entitled “Protease Inhibitors for the Treatment of HIV/AIDS: Recent Advances and Future Challenges”, Dr. Chandrashekhar Voshavar have discussed the recent development of novel small molecule-based inhibitors, their essential pharmacokinetic properties, and application in HAART on the horizon for targeting HIV-1 protease [6].

The review “Recent Progress in the Development of HIV-1 Entry Inhibitors: From Small Molecules to Potent Anti-HIV Agents” summarizes the advancement of HIV-1 entry inhibitors including new drug formulations and variations in the lead compounds for the development of novel inhibitors to increase ART treatment efficacy. HIV-1 entry inhibitors block one of the three steps of HIV invasion into host cells- attachment through CD4 receptor binding, association of co-receptor such as CCR5 and CXCR4 and finally the fusion process. Dr. Suttisintong and co-authors highlighted the computational modeling and structural modification approaches used for the development and screening of newer class of HIV-1 entry inhibitors to increase the potency and effectiveness of HIV treatment [7].

Dr. Maeda et al. in the article “Discovery and Development of anti-HIV Therapeutic Agents: Progress Towards Improved HIV Medication” discussed the discovery process of different types of inhibitors used in cART incorporating the FDA-approved anti HIV drugs and the improvement of the Quality Of Life (QOL) of patients. It also shines a spotlight on the future direction for the identification of novel treatment strategies and targets to overall block the HIV replication in host cells [8].

The envelope glycoprotein gp120 plays an important role in membrane fusion process of HIV host cell entry. Gp120 acts as a key player in the HIV life cycle as its interaction with CD4 triggers membrane fusion and one of its hypervariable loops help HIV to preferentially target T-cell or macrophages. Therefore, targeting gp120 for antiretroviral therapeutics has been a prime focus for researchers to prevent fusion of HIV with host cells. In the article “The Discovery and Development of Oxalamide and Pyrrole Small Molecule Inhibitors of gp120 and HIV Entry-a Review” Dr. Motati and co-authors have specifically elaborated the design and synthesis of biologically active class of oxalamide and pyrrole-containing compounds as potential inhibitors for gp120 [9].

Overall, the thematic issue focuses on the recent development of different approaches and strategies implicated to identify novel small molecule antiretroviral drugs for HIV treatment. We, as the Guest Editors would like to extend our sincere gratitude and appreciation to all the authors for their valuable contribution in this thematic issue.
REFERENCES

[1] Centre for Disease Control and Preventive (Available at: www.cdc.gov).


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