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# Effect of Phytocannabinoids in the Modulation of Thrombosis and Haemostasis

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During lead identi cation and optimization, the advancement criteria may be driven based on scienti c principles, prior experiences, and/or by examining the path paved by approved drugs. However, accessing the discovery data on physicochemical and ADME properties of the approved kinase inhibitors is a monumental task as these are either scattered in the literature or have not been published.

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1) To compile the relevant data on all kinase inhibitors approved prior to 2016 for easy access by the biopharmaceutical community, 2) To provide a retrospective analysis to highlight trends and attributes which may have contributed to the "developability" of these drugs, and 3) To ignite focused debates on what constitutes "actionable", "nice-to-have", and unnecessary data. Such debates bring about more clarity on stage appropriateness of di erent types of information and prevent confusion due to abundance of unnecessary data, leading to more e cient and less costly drug discovery programs.

e Philadelphia Chromosome was the result of reciprocal translocation of chromosomes 9 and 22, generating an elongated chromosome 9 and a truncated chromosome 22. e translocation juxtaposes the Abl1 gene on chromosome 9 to a part of the BCR on chromosome 22 and leads to CML. e translocated Abl1 gene, which encodes a tyrosine kinase, causes deregulated and continual overexpression of kinase activity resulting in tumor development. From this landmark discovery, it became evident that many human malignant diseases were associated with mutations, chromosomal rearrangements and/or overexpression of protein kinases [11, 13-16]. is discovery quickly led to protein kinases becoming well accepted targets for anticancer drug development [17-24]. During late 1980s and early 1990s, tremendous e orts were made to unfold the intracellular signal transduction pathways and aberrations of signaling pathways leading to variety of diseases at the genetic and molecular levels [25-30]. Many extra- and intra-cellularly associated kinases, such as MAPK, ERK, JAK and PI3K, were reported to regulate normal cellular functions [31, 32]. So far, a total of 518 human kinases and 900 human genes encoding for kinase proteins have been revealed [33]. In the meantime, it has been discovered that deregulation and/or over-expression of certain types of kinases lead to changes in the normal cellular functions which further advance to disease states. Platelets are small circulating blood cells that play primary roles in the maintenance of haemostasis through blood clotting. Inappropriate activation of platelets in pathological conditions results in thrombosis under arterial circulation causing an obstruction of the blood ow to major organs like heart and brain resulting in myocardial infarction and stroke, respectively. While the currently used anti-platelet drugs help saving lives, they're related to unwanted side e ects. Hence, the event of improved therapeutic strategies to treat/prevent thrombotic diseases may be a pressing priority. Non-psychoactive phytocannabinoids like cannabidiol (CBD) from marijuana plant are demonstrated to possess numerous bene cial e ects in distinctive pathological conditions.

erefore, during this study, we investigated the consequences of CBD and its precursor molecule cannabigerol (CBG) within the modulation of platelet function, thrombosis and haemostasis. Both CBD and CBG (at concentrations of 1-100µM) inhibited signi cantly agonists utilized in this study (CRP-XL, thrombin,

were employed.

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In conclusion, we have compiled physicochemical and ADME data on the rst 30 approved kinase inhibitors and provided our retrospective analysis, which we hope is helpful in constructing advancement criteria in discovery programs. e examination of this data provides an opportunity to develop an opinion on data prioritization and stage appropriateness of assays.

Note: This work is partly presented at 16th Global Summit on Toxicology & Applied Pharmacology October on 15-16, 2018 held at Las Vegas, USA