



WI-2-60-1-6

JOMO KENYATTA UNIVERSITY OF AGRICULTURE AND TECHNOLOGY
University Examinations 2021/2022

YEAR I SEMESTER I SPECIAL/SUPPLEMENTARY EXAMINATION FOR THE
DEGREE OF MASTER OF SCIENCE IN MEDICINAL CHEMISTRY

TPS 3100: QUANTITATIVE STRUCTURE ACTIVITY RELATIONSHIPS

DATE: AUGUST, 2022

TIME: 3 HOURS

1. Using dementia (a central nervous system degenerative condition) and malaria as case studies, discuss how disease niche drives the medicinal chemistry plan for lead optimization.
2. Consider the presumptive lead whose structure is given in **Figure 1**, intended for the treatment of malaria. Propose structural modifications that could deliver an optimized lead.

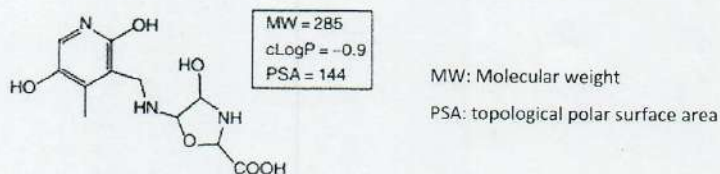


Figure 1: Presumptive antimalarial lead

3. Discuss the application of Lipinski's propositions, popularly termed *Lipinski Rule of 5*, in drug discovery.
4. Using specific examples, illustrate how modifying the ionization characteristics of a lead compound can impact on its pharmacokinetics and pharmacodynamics.
5. Discuss how solubility of the drugs in **Figure 2** can be determined in a drug discovery laboratory and compare the solubility of the drugs at neutral pH (intrinsic solubility) and at pH 9.

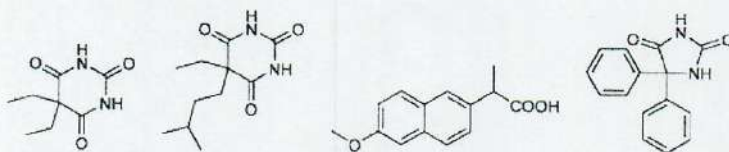


Figure 2: Structures of clinically useful drugs

6. Describe the utility of the biopharmaceutics classification system of compounds in drug discovery.