KENYATTA UNIVERSITY

UNIVERSITY EXAMINATIONS 2011/2012

SECOND SEMESTER EXAMINATION FOR THE DEGREE OF BACHELOR OF SCIENCE DEGREE IN MOLECULAR CELL BIOLOGY
SBC 406: PHARMACEUTICAL CHEMISTRY

DATE: Wednesday 28th March, 2012 **TIME:** 4.30 p.m. – 6.30 p.m.

***INSTRUCTIONS*: ANSWER ALL QUESTIONS IN SECTIONS "A" AND "B" COMPULSORY) AND ANY OTHER TWO QUESTIONS IN SECTION C**

SECTION A:Answer ALL the Questions (20 marks)

1. The following passage on rational drug development process is incomplete. Fill in the missing gaps with appropriate terms commonly encountered in this field. (5 marks)

In virtual, biochemical and cell-based testing, compound selections are run against an isolated or physiologically embedded target that may be involved in the disease process. A compound that exceeds a certain threshold value in binding to the target or modulation of some functional signal behind it is called a _____. If the identity and purity of the compound and the assay results are confirmed in a multipoint activity determination, the compound raises to the status of _____. This is in turn developed in to a _____, which is a compound with proven activity and selectivity. Molecular modification tunes the physicochemical parameters of the compound so that it becomes suitable for ADME, and the compound is termed as an _____ or *preclinical candidate*. If this displays no toxicity in cell and animal models, it becomes a _____. If this stands the tests of efficacy and safety in humans and overcomes marketing hurdles, a *new drug entity* will enter the treasure trove of pharmacy.

2. List the 3 main steps involved in the drug discovery and development process. (3 marks)

a) _____

b) _____

c) _____

3. In selecting drugs for the treatment of infections due to invading parasites or pathogens the guiding principle of _____ ensures that the drug is maximally harmful to the parasite but minimally harmful to the infected patient. (1 mark)

4. List 4 molecular or cellular drug targets via which drugs mediate their therapeutic effects. (4 marks)

a) _____

b) _____

c) _____

d) _____

5. List the 4 main hit or lead finding strategies during the search for new drugs. (4 marks)

a) _____

b) _____

c) _____

d) _____

6. List any three limitations of conventional chemotherapeutic agents that are currently used in the management of human diseases? (3 marks)

a) _____

b) _____

c) _____

SECTION B: Answer ALL Questions (30 Marks)

1. Briefly explain the following techniques used in modern discovery of novel medicines in pharmaceutical industry.

(i) High throughput screening. (3 marks)

(ii) Combinatorial chemistry. (2 Marks)

2. Almost 30% of all marketed drugs act on GPCRs. Briefly explain the structure and characteristics of G-proteins. (5 marks)

3a). Explain the term "rational drug design? (2 marks)

b). List three human diseases that have benefited immensely from rational drug design approach with novel therapeutics already in clinical use. (3 marks)

4. Once a hit is discovered, its activity must be confirmed and validated. State 5 typical hit validation criteria necessary before it is qualified to a lead. (5 marks)

5. Explain the term "pharmacophore" as used in medicinal chemistry. (5 marks)

6. Explain the fundamental difference between fragment-based drug discovey (FBDD) and high-throughput screening/Hit-To-Lead (HTS/HTL) approaches of drug design. (5 marks)

SECTION C: Answer ANY TWO Questions (20 marks)

1. Once a new drug molecule has been synthesized, one has to verify that it possesses the functional activity and therapeutic efficacy expected. Briefly explain three biological tests that are included in a screening architecture, and list the nature of information that can be deduced from each. (10 marks)

2. The most popular strategy used in finding hits or leads in the drug discovery process is "analog design". Briefly discuss and list two advantages and one disadvantage of the approach. (10 marks)

3. Briefly explain the main phases of clinical investigation of drugs during drug development process. (10 marks)