

## CASE STUDY BASED PUZZLE

## BP807ET:COMPUER AIDED DRUG DESIGN

## UNIT 1: ANALOG BASED DRUG

DESIGN:BIOISOSTERISM, CLASSIFICATION,

BIOISOSTERIC REPLACEMENT. ANY THREE

CASE STUDIES

## Case Study Puzzle 1

### Bioisosterism – Concept & Classical Bioisosteres

#### Case Scenario

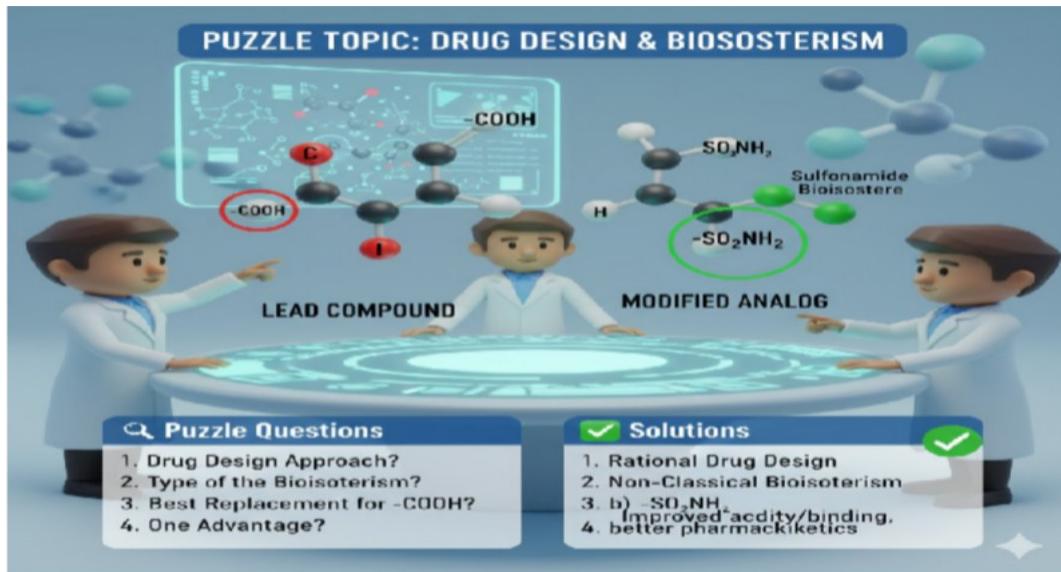
A pharmaceutical company is developing an oral anti-inflammatory drug.

The lead compound shows good activity, but causes gastric irritation due to the presence of a –COOH (carboxylic acid) group.

To reduce gastric side effects while retaining activity, the medicinal chemist replaces the –COOH group with another functional group of similar size and electronic properties.

#### Puzzle Questions

1. Identify the drug design approach used in this modification.
2. What type of bioisosterism is applied here?
3. Choose the best bioisosteric replacement for –COOH:
  - a) –NH<sub>2</sub>
  - b) –SO<sub>2</sub>NH<sub>2</sub>
  - c) –CONH<sub>2</sub>
  - d) –CH<sub>3</sub>
1. State one advantage of this bioisosteric replacement.



## Case Study Puzzle 2

### Classification of Bioisosteres

#### Case Scenario

A known antibacterial drug contains a  $-\text{H}$  atom at a position crucial for activity. However, the drug is rapidly metabolized in the liver, reducing its duration of action. The medicinal chemist replaces  $-\text{H}$  with  $-\text{F}$  (fluorine) to improve metabolic stability without significantly altering biological activity.

#### Puzzle Questions

1. Why is fluorine considered a suitable replacement for hydrogen?
2. Classify the  $\text{H} \rightarrow \text{F}$  replacement as:
  - a) Non-classical bioisostere
  - b) Classical bioisostere
  - c) Isomeric replacement
  - d) Prodrug approach
1. Which property is improved by this replacement?
  - a) Taste
  - b) Metabolic stability
  - c) Solubility
  - d) Color
1. Name one example drug where fluorine substitution improves activity or stability.



## Case Study Puzzle 3

### Bioisosteric Replacement in Drug Optimization

#### Case Scenario

A lead compound developed for antihistaminic activity contains a phenyl ring.

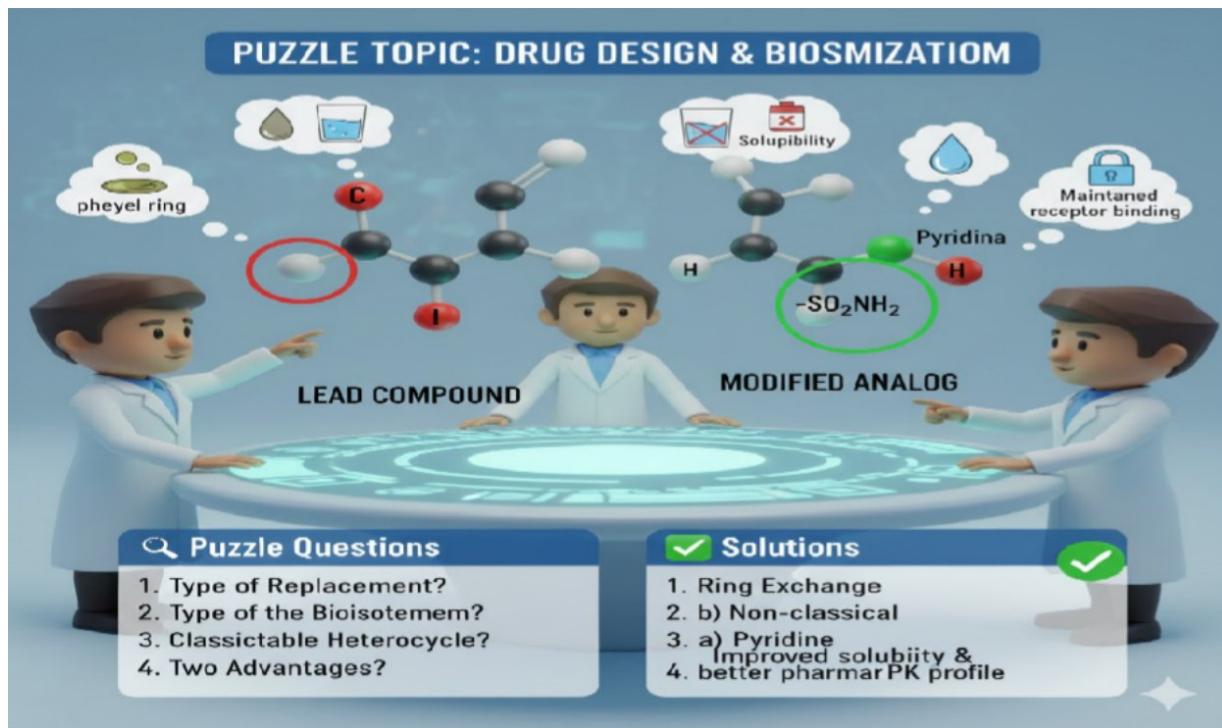
Although potent, the compound shows high lipophilicity, causing poor water solubility.

To improve solubility while maintaining receptor binding, the chemist replaces the phenyl ring with a heterocyclic ring.

#### Puzzle Questions

1. What type of bioisosteric replacement is being performed?
2. Identify the classification of this bioisostere:
  - a) Classical
  - b) Non-classical
3. Which heterocycle is most suitable as a phenyl bioisostere?
  - a) Pyridine
  - b) Cyclohexane
  - c) Ethane
  - d) Methane
4. Mention two advantages of this replacement.

**PUZZLE TOPIC: DRUG DESIGN & BIOSMIZATION**



**LEAD COMPOUND**

**MODIFIED ANALOG**

**Puzzle Questions**

1. Type of Replacement?
2. Type of the Bioisotemem?
3. Classictable Heterocycle?
4. Two Advantages?

**Solutions**

1. Ring Exchange
2. b) Non-classical
3. a) Pyridine  
Improved solubiility &
4. better pharmarPK profile