

CASE STUDY BASED PUZZLE

BP807ET: COMPUTER 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

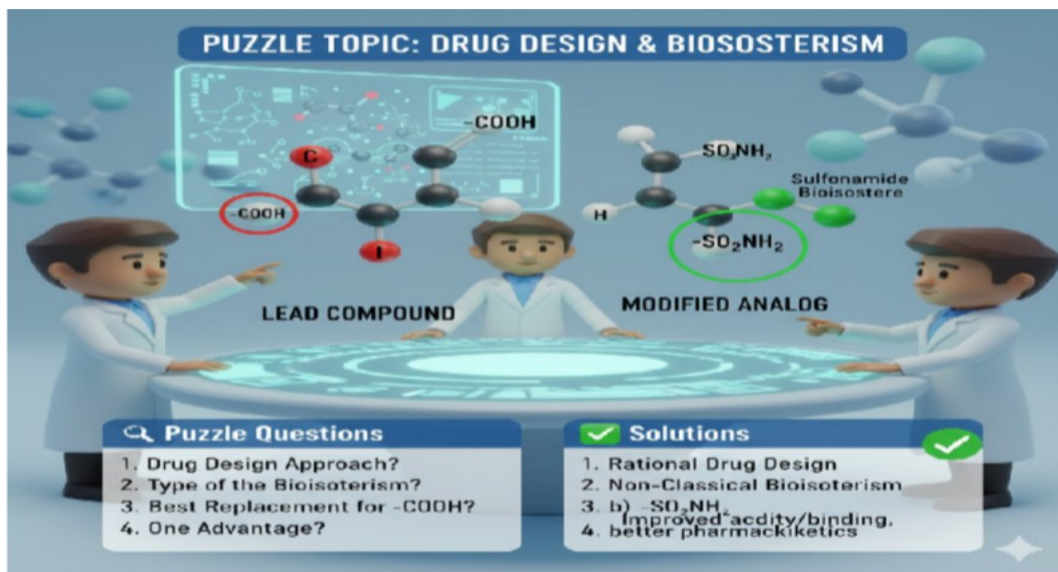
A pharmaceutical company is developing an oral anti-inflammatory drug.

The lead compound shows good activity, but causes gastric irritation due to the presence of a $-\text{COOH}$ (carboxylic acid) group.

To reduce gastric side effects while retaining activity, the medicinal chemist replaces the $-\text{COOH}$ 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 $-\text{COOH}$:
 - a) $-\text{NH}_2$
 - b) $-\text{SO}_2\text{NH}_2$
 - c) $-\text{CONH}_2$
 - d) $-\text{CH}_3$
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

Thought bubbles for Lead Compound: phenyl ring, Solubility (marked with a red X), Maintained receptor binding (marked with a red X).

Thought bubbles for Modified Analog: Pyridine, Solubility (marked with a green checkmark), Maintained receptor binding (marked with a green checkmark).

Puzzle Questions	Solutions
1. Type of Replacement?	1. Ring Exchange
2. Type of the Bioisotemem?	2. b) Non-classical
3. Classictable Heterocycle?	3. a) Pyridine
4. Two Advantages?	Improved solubiity & better pharma PK profile