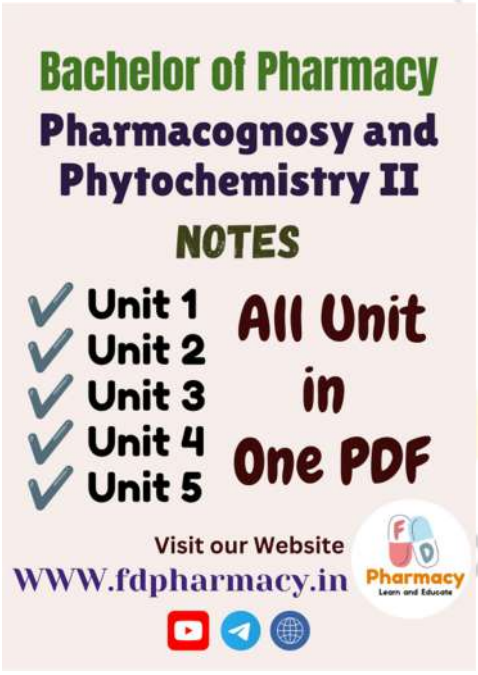
WELCOME

TO


Bachelor of Pharmacy
Pharmaceutical Jurisprudence
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate


Bachelor of Pharmacy
Industrial Pharmacy I
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate


Bachelor of Pharmacy
Medicinal Chemistry II
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate


Bachelor of Pharmacy
Pharmacognosy and Phytochemistry II
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate


Bachelor of Pharmacy
Pharmacology II
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate

MEDICINAL CHEMISTRY - II

UNIT 5

TOPIC :

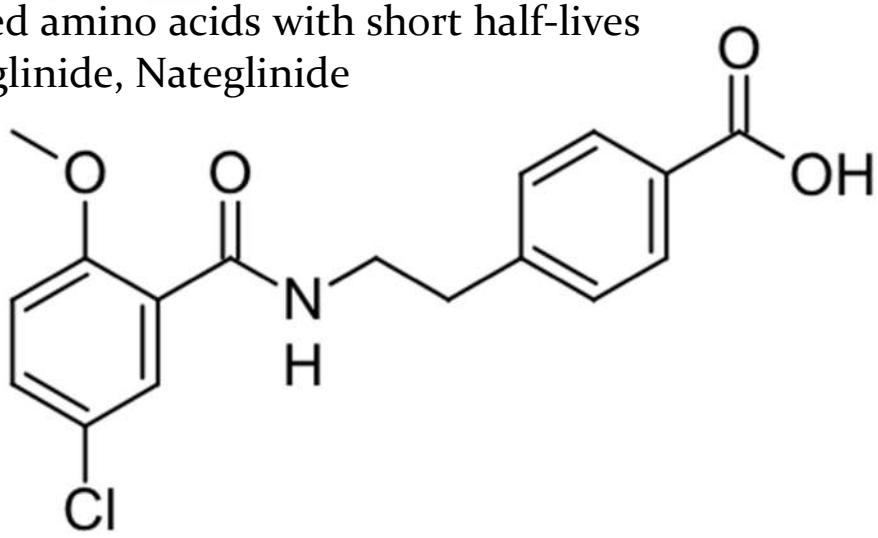
- **Meglitinides :** Repaglinide, Nateglinide.

Meglitinides

- Meglitinides are a class of oral antidiabetic agents used in Type 2 Diabetes Mellitus (T2DM).
- They are rapid-acting insulin secretagogues that help control postprandial hyperglycemia.
- Often used in patients who cannot tolerate sulfonylureas or have irregular meal schedules.

Chemical Structure

- Non-sulfonylurea insulin secretagogues
- C-aryl substituted amino acids with short half-lives
- Examples: Repaglinide, Nateglinide



Mechanism of Action

1. Bind to ATP-sensitive K^+ channels on pancreatic β-cells (different binding site than sulfonylureas)
2. Close K^+ channels → membrane depolarization
3. Opening of voltage-gated Ca^{2+} channels → Ca^{2+} influx
4. Stimulates rapid, short-duration insulin secretion in response to meals

Key point: Effect is glucose-dependent, so lower risk of hypoglycemia compared to sulfonylureas.

Clinical Uses

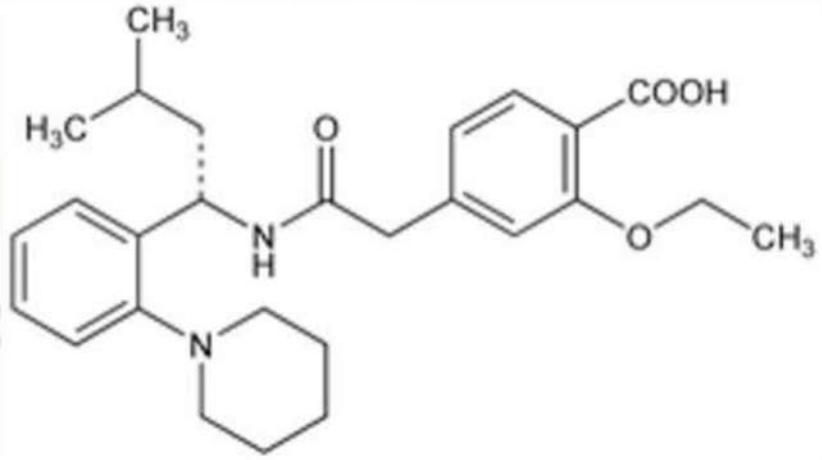
- Type 2 Diabetes Mellitus (particularly postprandial hyperglycemia)
- Combination therapy: Often used with Metformin for synergistic effect
- Useful in patients with irregular meals or risk of hypoglycemia with sulfonylureas

Repaglinide

- Repaglinide is a meglitinide class oral hypoglycemic agent.
- Used to treat type 2 diabetes mellitus, particularly postprandial hyperglycemia.
- It is rapid-acting with a short duration of action (about 4–6 hours), allowing dosing before meals.
- Administered orally, usually 0–30 minutes before a meal.
- Advantages: Rapid onset, low risk of prolonged hypoglycemia, flexible dosing with meals.

Chemical Structure

- Chemical name: 2-ethoxy-4-[2-(3-methyl-1-(2-(1-piperidinyl)phenyl)butyl)phenyl]benzoic acid
- Molecular formula: $C_{22}H_{28}N_2O_4$
- Molecular weight: 452.48 g/mol
- Chemical class: Meglitinide; oral hypoglycemic agent
- Structural



Mechanism of Action

- Primary Target: Pancreatic β-cells (ATP-sensitive K^+ channels)

Stepwise Mechanism:

1. Repaglinide binds to specific sites on SUR1 receptor on β-cell plasma membrane.

2. Closes ATP-sensitive K^+ channels, causing membrane depolarization.
3. Depolarization opens voltage-dependent Ca^{2+} channels, increasing intracellular calcium.
4. Calcium triggers rapid exocytosis of insulin-containing granules.
5. Overall Effect:
    - Rapid insulin release after meals → reduces postprandial glucose
    - Short duration minimizes prolonged hypoglycemia

Note: Unlike sulfonylureas, Repaglinide has mealtime-specific action with less risk of fasting hypoglycemia.

Synthesis

1. Starting materials: Substituted benzoic acids and phenylpropyl derivatives
2. Step 1: Formation of the central phenyl-propyl skeleton
3. Step 2: Introduction of piperidinyl moiety via amide formation
4. Step 3: Purification → crystallization to obtain pharmaceutical-grade Repaglinide

Uses

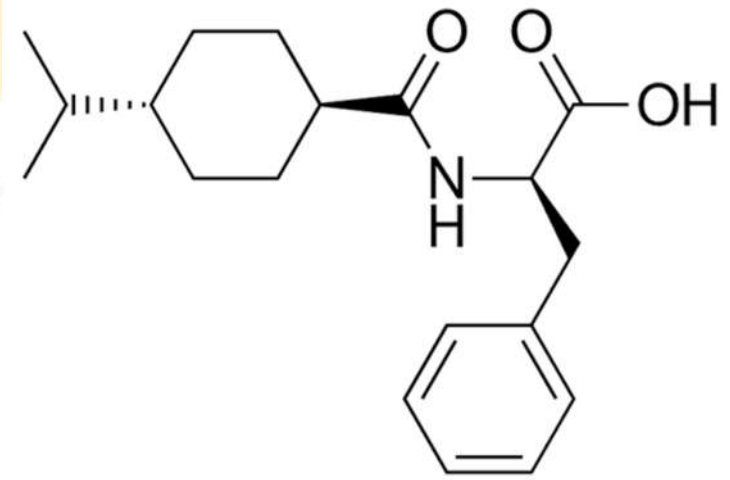
- Therapeutic Uses:
    1. Type 2 diabetes mellitus (especially postprandial hyperglycemia)
    2. Can be used alone or in combination with metformin

Nateglinide

- Nateglinide is a meglitinide class oral hypoglycemic agent, similar to repaglinide.
- Used for type 2 diabetes mellitus, specifically to control postprandial hyperglycemia.
- Rapid-acting with short duration (about 4–5 hours), taken before meals.
- It stimulates insulin release in a glucose-dependent manner, minimizing risk of prolonged hypoglycemia.
- Administered orally, usually 0–30 minutes before a meal.

Chemical Structure

- Chemical name: 2-cyano-3-(N-phenylacetamido)-N-(2-isopropyl-phenyl)propanamide
- Molecular formula: $C_{22}H_{24}N_4O_2$
- Molecular weight: 380.46 g/mol
- Chemical class: Meglitinide; oral hypoglycemic agent
- Structural



Mechanism of Action

- Primary Target: Pancreatic β-cells (ATP-sensitive K^+ channels)

Stepwise Mechanism:

1. Nateglinide binds to specific sites on SUR1 receptor on β-cell plasma membrane.
2. Closes ATP-sensitive K^+ channels, causing membrane depolarization.
3. Depolarization opens voltage-dependent Ca^{2+} channels, increasing intracellular calcium.
4. Calcium triggers exocytosis of insulin-containing granules.
5. Overall Effect:
    - Rapid insulin release after meals → reduces postprandial glucose
    - Short duration → minimal risk of prolonged hypoglycemia

Note: Glucose-dependent action reduces fasting hypoglycemia risk compared to sulfonylureas.

Synthesis

1. Starting materials: Substituted phenylpropyl derivatives and cyanoacetamide
2. Step 1: Formation of central phenylpropyl skeleton
3. Step 2: Amide bond formation with phenylacetamido group
4. Step 3: Purification → crystallization to obtain pharmaceutical-grade Nateglinide

Uses

- Therapeutic Uses:
    1. Type 2 diabetes mellitus (particularly postprandial hyperglycemia)
    2. Can be used alone or in combination with metformin