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New Synthetic Strategies for The Preparation of Bioactive Molecules

طالب الماجستير

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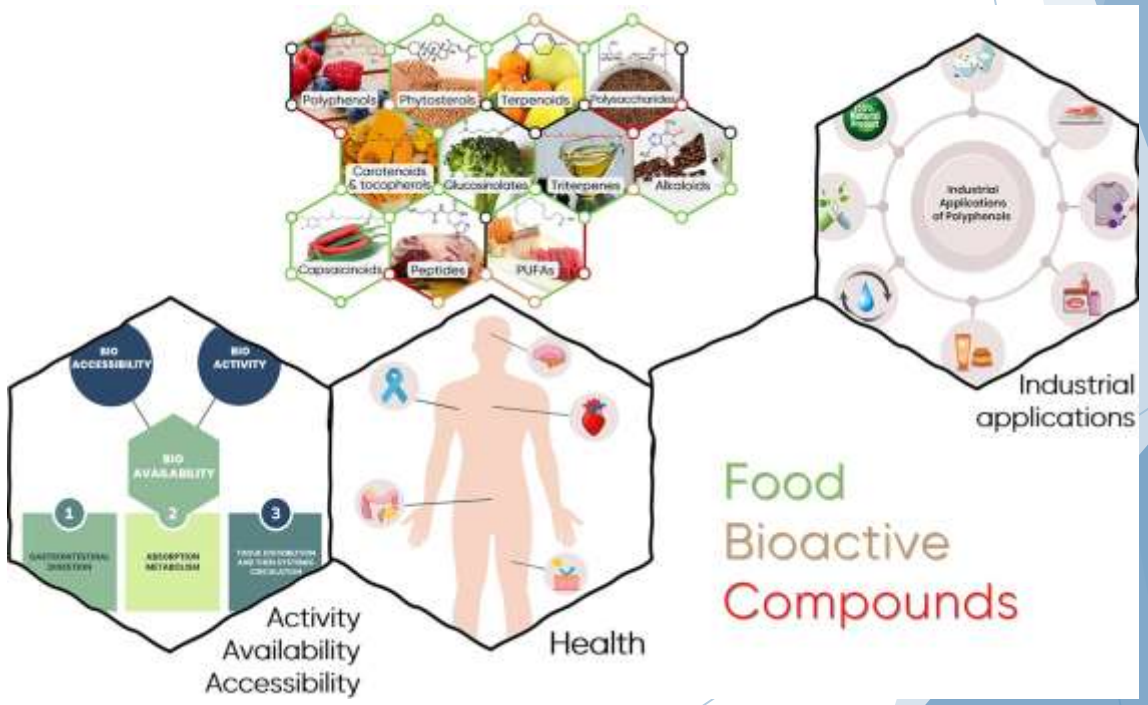
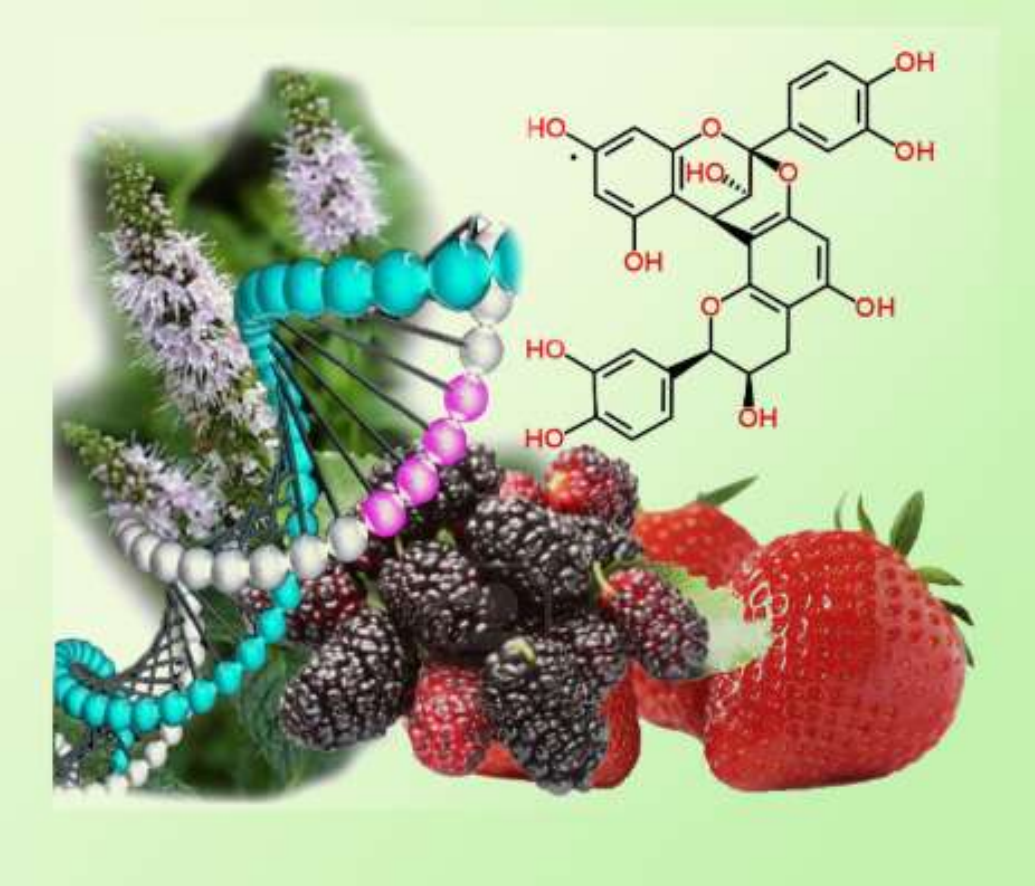


Bioactive Molecules

- **Bioactive molecules**, Bioactive molecules are compounds that elicit biological effects on living organisms, playing a crucial role in health and disease processes.
  - **These compounds** are typically found in small quantities within various foods, particularly in plants, and they can influence health and disease outcomes.
  - The term "**bioactive**" is synonymous with "**biologically active**," indicating that these substances can interact with biological systems to produce a range of effects.



Characteristics of Bioactive Molecules

- **Source**: Bioactive compounds are primarily derived from natural sources, They encompass a variety of chemical classes, such as:

Alkaloids: Naturally occurring compounds, often with significant pharmacological effects, such as morphine used for pain relief.

Terpenoids: Diverse group known for their aromatic properties, exemplified by Taxol, an important anticancer drug.

Flavonoids: Plant-derived compounds like quercetin, recognized for their antioxidant properties and potential health benefits.

- **Biological Activity**: These molecules can exert beneficial effects on human health, including :

Antioxidant activity, Anti-inflammatory properties, Modulation of metabolic processes, and others.

Importance of bioactive molecules in Drug Discovery

- Bioactive molecules serve as critical leads in drug discovery, aiding in the development of new therapeutic agents aimed at treating various diseases, including cancer, cardiovascular diseases, and infectious diseases.
- With advances in biotechnology and pharmacology, bioactive molecules will continue to be pivotal in discovering innovative treatments and enhancing existing therapeutic strategies.

Synthetic Strategies for The Preparation of Bioactive Molecules

- **Traditional Synthetic Strategies**
  - chemical
  - Extraction from natural sources
- **New synthetic Strategies**
  - Biotechnological Methods
  - New Chemical methods
    - Green chemistry
    - Click chemistry
    - Flow chemistry
  - Computational Methods

Traditional Synthetic Strategies

- Traditional synthetic strategies refer to the established methods used for decades in the field of organic chemistry.
- These strategies primarily focus on the synthesis of organic compounds through various techniques that have proven effective over time.

Traditional Synthetic Strategies

1.Chemical Synthesis:

- This involves the stepwise assembly of molecules through **established** organic chemistry techniques.
- This strategy often rely on the use of **reagents** and **catalysts** to facilitate reactions.
- They are sometimes lead to **complex mixtures** and **require extensive purification processes.**
- **Offers greater flexibility** in designing synthetic routes, allowing chemists to create a wide range of compounds.

Continue

The mostly involved chemical reaction types are :

A- Nucleophilic Substitution:

- It is crucial in organic chemistry for constructing complex molecules .
- It enables the creation of diverse functional groups.

B- Coupling reactions:

• Coupling reactions, such as Suzuki and Heck reactions, are fundamental for linking two molecular fragments together.

•These reactions are widely used in drug discovery to create larger and more complex structures.

C- Functional Group Transformations:

•It is vital for modifying the physical and chemical properties of organic compounds. The oxidation, reduction, and hydrolysis are employed to achieve desired characteristics in target molecules.

2- **Extraction from Natural Sources**:

Bioactive compounds have historically been isolated from plants, fungi, and other natural sources using techniques like:

A- **Soxhlet extraction**: it is involved continuous extraction using a cycle solvent evaporation and condensation.

B- **Maceration**: It is involve soaking the source material in solvent and allow the bioactive compounds to diffuse to the solvent over time.

C- **Hydro-distillation** : the solvent used is only water .

Advantages of traditional strategies

- These methods are backed by decades of research, offering reliable and reproducible pathways.
- These are often yield high-purity compounds, which are essential for applications in pharmaceuticals where purity is paramount.

Disadvantages of traditional strategies

- Traditional synthesis methods can be time-consuming and require extensive resources.
- The use of hazardous reagents and conditions poses safety risks and environmental concerns, necessitating careful management.

New synthetic Strategies

New synthetic strategies

- refer to innovative methods that utilize advancements in technology and chemistry to enhance the process of chemical synthesis.
- These strategies aim to **create more efficient, sustainable,** and **safer chemical products.**

New synthetic Strategies

1- Biotechnological Methods :

This strategy is rely on the generation of novel bioactive molecules by manipulating biosynthetic pathways in microorganisms, such as :

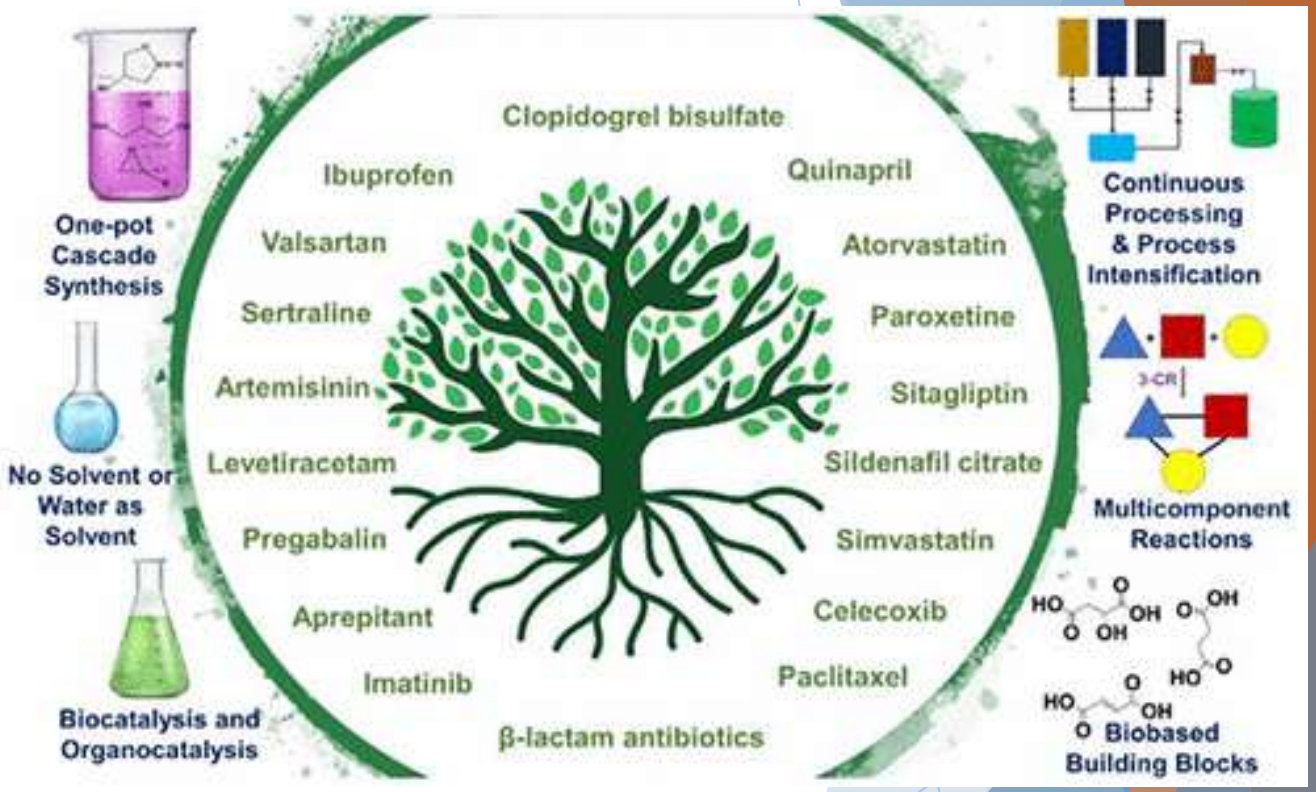
A. **Combinatorial biosynthesis** is a powerful approach that integrates various biosynthetic pathways to create novel compounds. By utilizing genetic and biochemical engineering, researchers can manipulate microorganisms to produce a wider array of bioactive molecules than traditional methods allow.

B. **Mutasynthesis** : It refers to the innovative technique of utilizing mutated precursors to synthesize novel compounds.

2- New Chemical methods :

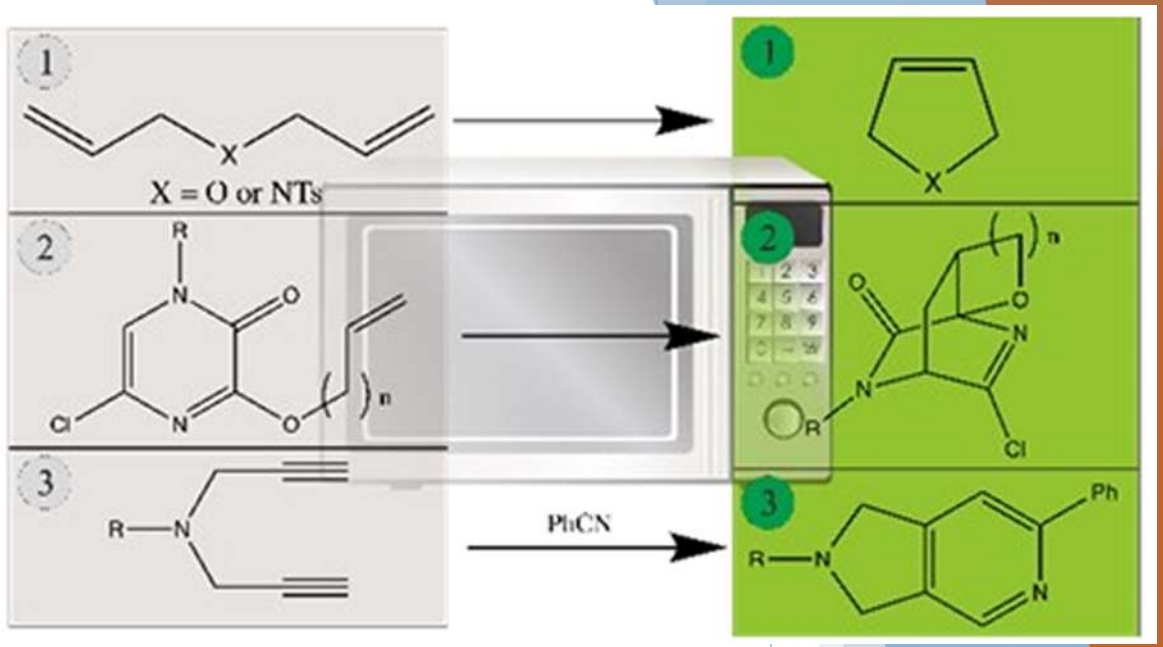
A- Green chemistry :

- focuses on designing chemical products and processes that minimize the use and generation of hazardous substances.
- This discipline aims to reduce environmental impact and enhance sustainability through various principles . Its principles: waste prevention, safer Chemicals, energy efficiency.
- Utilizing **innovative techniques** such as microwave synthesis and photocatalysis to enhance reaction efficiency .



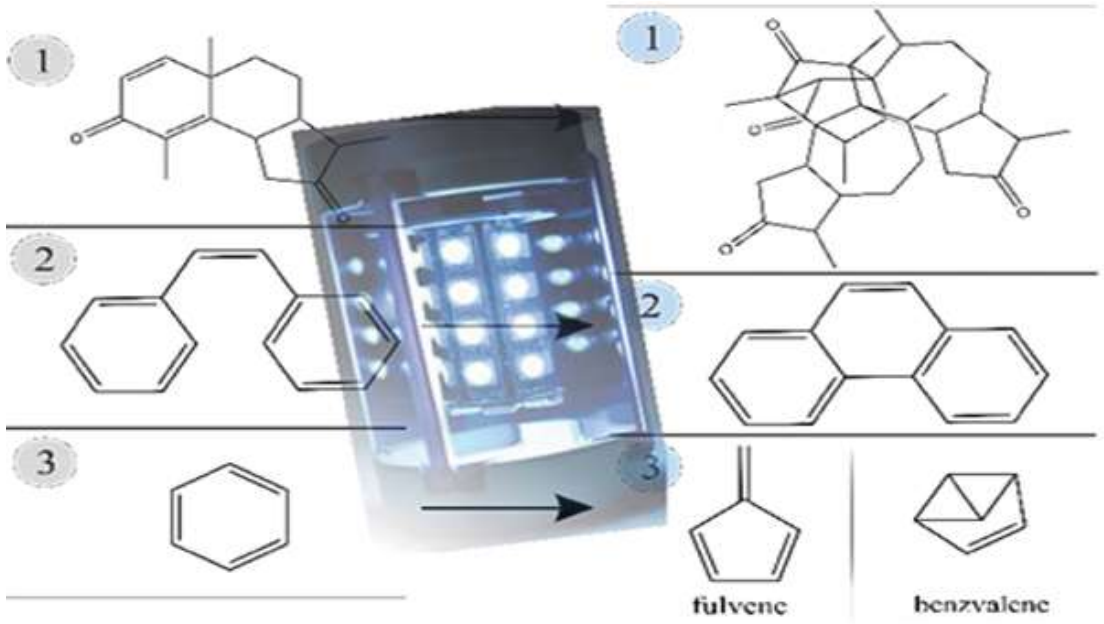
- Green chemistry Utilizing **innovative techniques** such as:
- microwave synthesis
- Photocatalysis

to enhance reaction efficiency .



Microwave-Assisted Organic Synthesis (MAOS) process for several organic reactions

- **MAOS** is applied for some organic reactions, such as ring-closing metathesis of diallyl derivatives, intramolecular hetero-Diels-Alder cycloaddition of alkenyl-tethered 2(1H)-pyrazolines, cyclotrimerization reaction between the diyne and benzonitrile, and so on

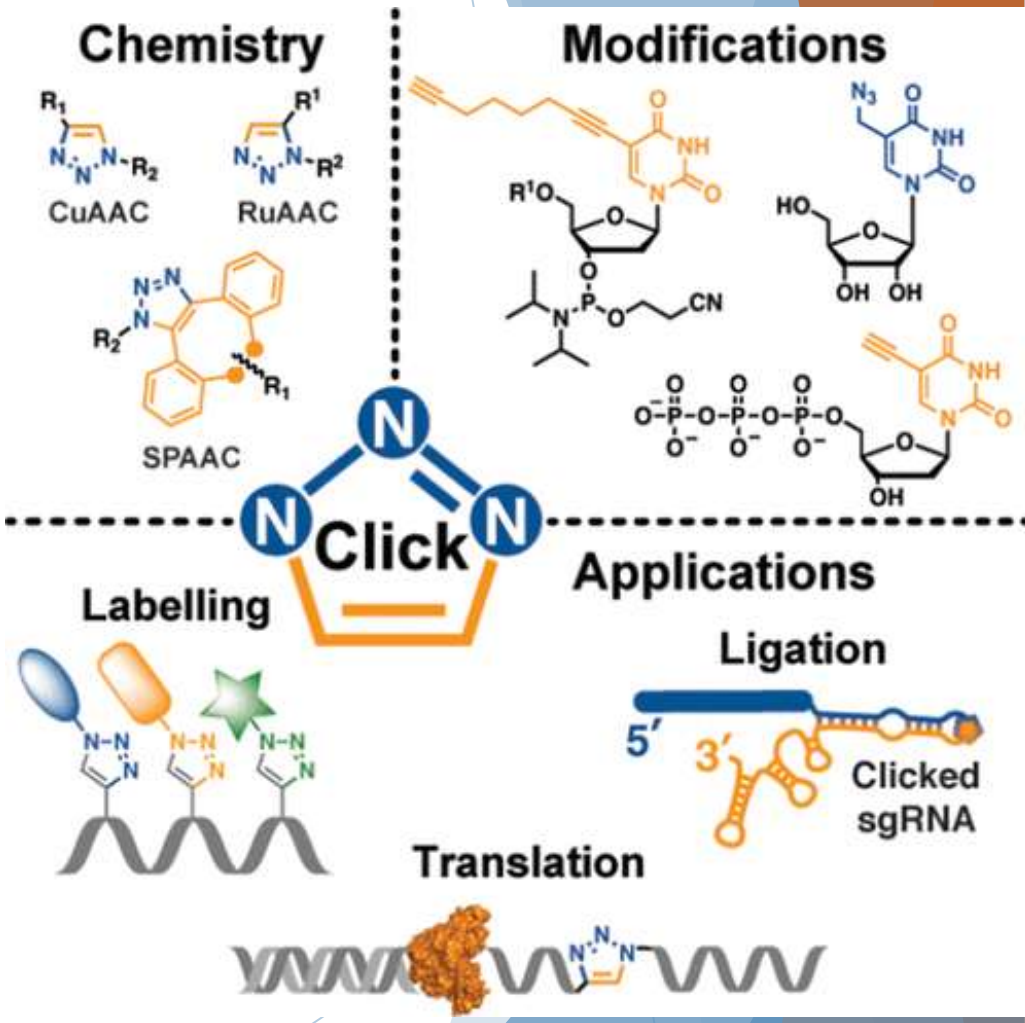


Photochemistry reaction for the production of organic compounds.

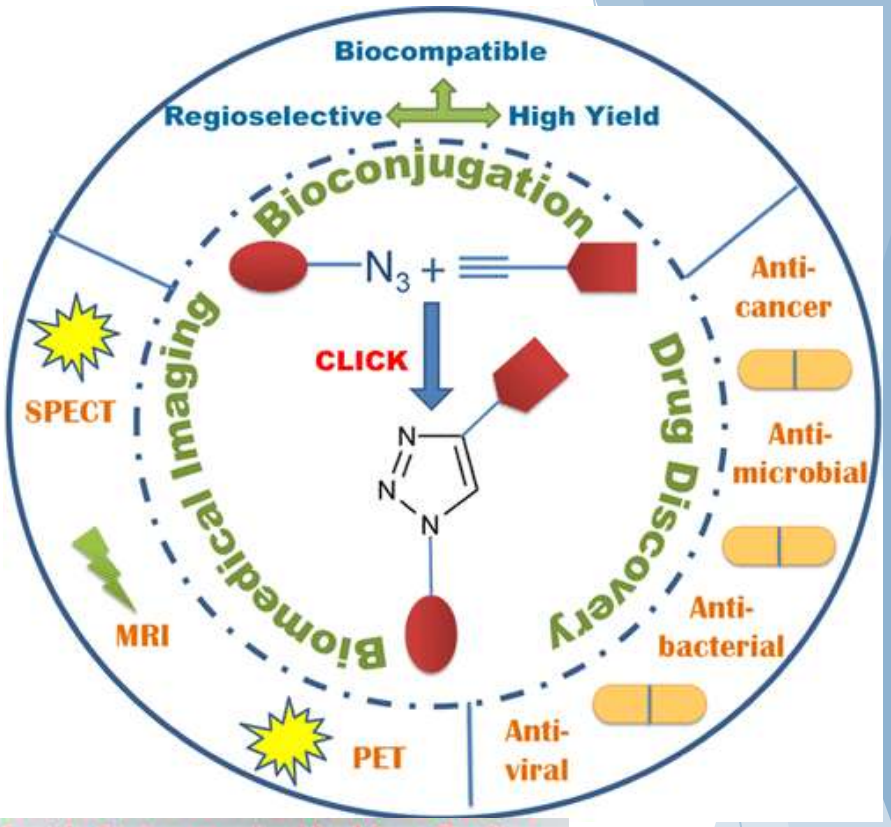
- The Claisen rearrangement, Diels Alder reaction, and other pericyclic reactions are examples **catalyzed photochemical reactions**

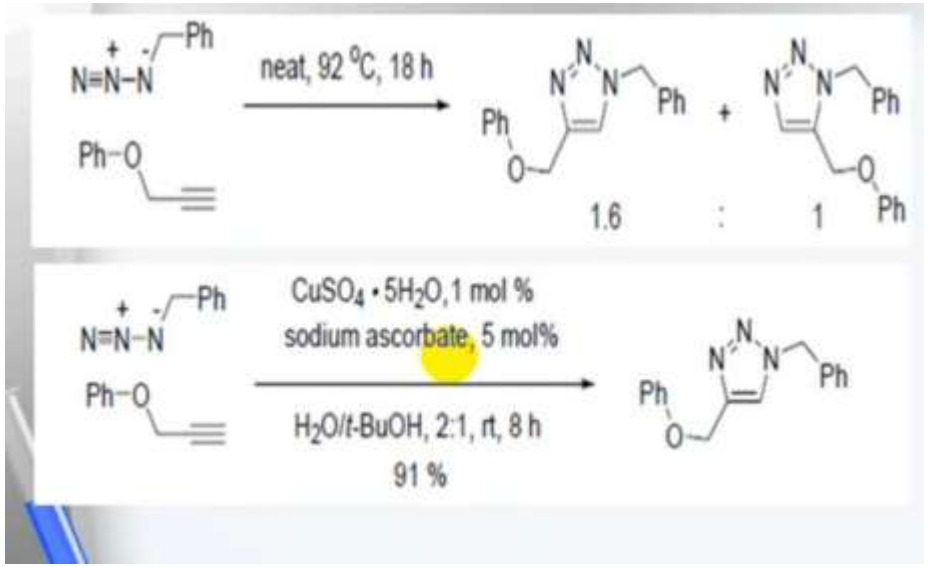
B- **Click Chemistry** :

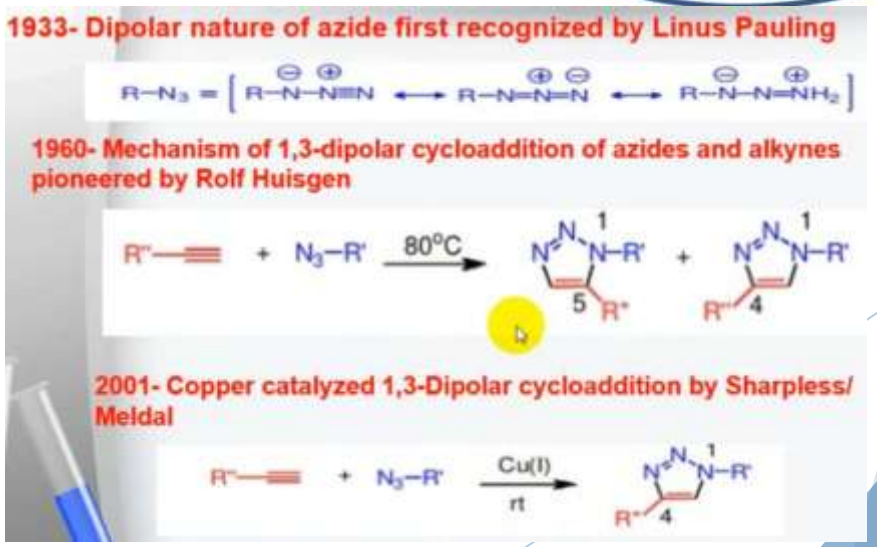
- It is a collection of chemical reactions that are characterized by their simplicity and high yield.
- This approach minimizes side reactions and produces products quickly and reliably, making it a preferred method in synthetic chemistry.
- Its primary reaction was the azide-alkyne cycloaddition which is highly efficient due to its ability to selectively form triazole rings, which are essential in various chemical applications, including drug development. Cu(I)-catalyzed azide−alkyne cycloaddition (CuAAC) is a modular and bio-orthogonal approach that is being adopted for the efficient synthesis of organic and bioorganic compounds.



Bioconjugation is one of the significant applications of Click Chemistry, where it helps in attaching biomolecules to drugs or imaging agents. This process enhances the functionality and targeting capabilities of pharmaceutical compounds, leading to improved therapeutic outcomes







C - Flow Chemistry:

- The principles of this a method are:

➢ The conduction chemical reactions in a **continuous flow system**, as opposed to traditional batch processing.

➢ It is provides a **more controlled environment** for chemical reactions.

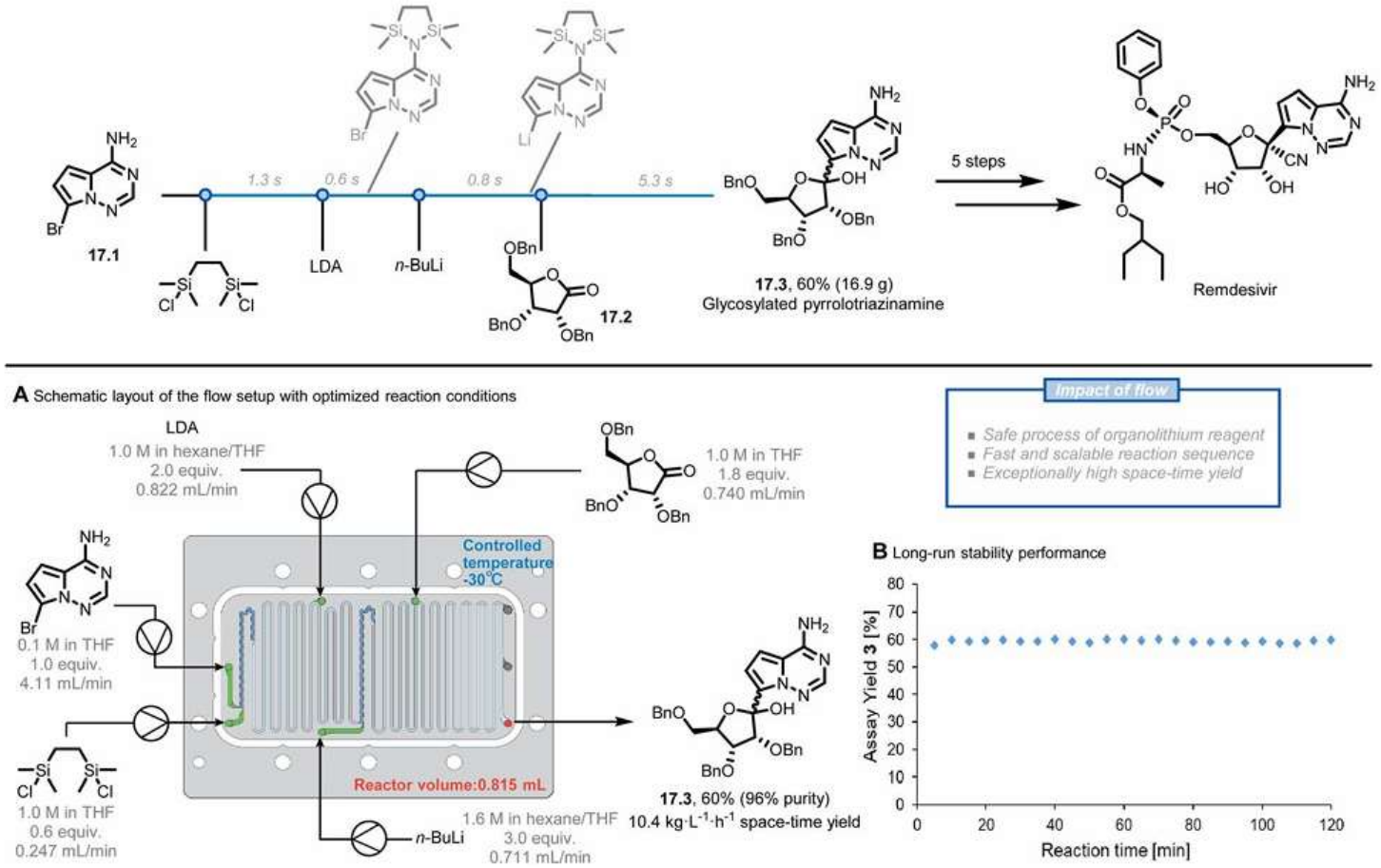
➢ **Scalability: It is** facilitates easier scaling up from laboratory experiments to industrial production.

➢ **Enhanced Safety:** Continuous flow systems allow for better heat and mass transfer, which reduces the risk of hazardous situations such as **overheating, pressure build-up, or uncontrolled reactions.**

➢ **Increased Reaction Efficiency:** The continuous nature of the process allows for optimized reaction conditions, leading to faster and more efficient chemical transformations.

Example of improve scalability by flow chemistry

- _Remdesivir, the first COVID-19 drug approved by the U.S. FDA



Continuous-flow process to generate remdesivir intermediates

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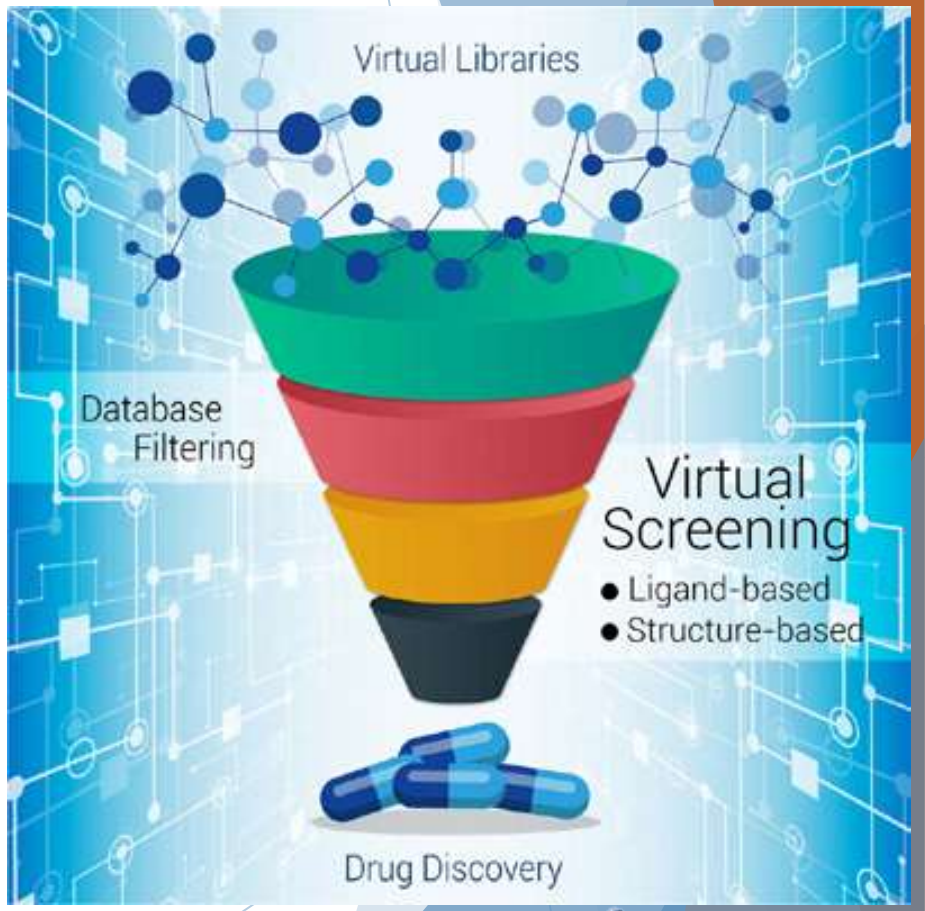
3-Computational Methods:

A- Virtual Screening (VS)

- Description: Virtual screening involves the computational evaluation of large libraries of compounds to identify those that are likely to interact with a specific biological target.
- Types:

- Structure-Based Methods: Utilize the 3D structure of the target protein to predict binding interactions (e.g., molecular docking).
- Ligand-Based Methods: Rely on known active compounds to identify new candidates based on similarity or quantitative structure-activity relationships (QSAR).

- Applications: VS has been instrumental in identifying lead compounds for various therapeutic targets, significantly accelerating the drug discovery process.



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B- Molecular Dynamics (MD) Simulations

- Description: MD simulations model the physical movements of atoms and molecules over time, providing insights into the dynamic behavior of biological systems.
- Applications: Used to study protein-ligand interactions, conformational changes, and the stability of drug candidates, aiding in understanding mechanisms of action and optimizing binding affinities.

C- Quantitative Structure-Activity Relationship (QSAR) Modeling

- Description: QSAR models correlate chemical structure with biological activity using statistical methods.
- Applications: Helps predict the activity of new compounds based on their structural features, guiding the design of more potent drugs.

D-Molecular Docking:

- Description: A computational technique that predicts how small molecules (ligands) bind to a receptor (usually a protein).
- Applications: Essential for identifying potential drug candidates and optimizing their interactions with biological targets.

E- Machine Learning and AI:

- Description: Advanced algorithms analyze large datasets to identify patterns and make predictions about molecular properties and activities.
- Applications: Enhances drug discovery by predicting ADMET (absorption, distribution, metabolism, excretion, toxicity) properties and optimizing lead candidates through data-driven approaches.

F- Pharmacophore Modeling:

- Description: Identifies the spatial arrangement of features necessary for a molecule to interact with a specific biological target.
- Applications: Used in virtual screening and lead optimization by focusing on key interactions critical for bioactivity.

Advantages of Computational Methods

- ✓ Cost Efficiency
- ✓ Time-Saving
- ✓ Enhanced Data Analysis
- ✓ Lower Experimental Failures
- ✓ Support for Novel Discoveries

Challenges and Limitations

- ➢ **Computational Resources:**

High computational demands pose a barrier to the widespread use of advanced computational methods.

- ➢ **Complexity of Biological Systems:**

Biological systems are inherently complex, involving numerous interacting components that can be difficult to model accurately.

- ➢ **Need for Improved Algorithms.**
- ➢ **Integration of Experimental Data.**

❖ **The integration of computational tools in drug discovery enhances the identification and optimization of bioactive compounds.**

New Synthetic Strategies Versus Traditional Synthetic Strategies

Resource use	• traditional: High use of solvents and reagents, leading to increased costs and waste • New: Lower resource use with the adoption of green solvents and minimal waste practices.
Time Efficiency	• Traditional : Processes are often lengthy, requiring more time for completion. • New : Generally faster processes, optimizing efficiency and throughput.
Safety	• Traditional: Potentially hazardous materials and processes, posing risks to users. • New : Generally safer approaches with reduced hazards and risks.
Scalability	• Traditional: Scalability often presents challenges due to complexity. • New: Easier scalability, allowing for more flexible and adaptable production.
Environmental Impact	• Traditional: Significant waste generation, contributing to environmental concerns. • New: A focus on sustainability, aiming to minimize environmental impact.

Conclusions

Traditional Synthetic Strategies

- **They** are established methods have been the backbone of chemical synthesis for decades.
- **They offer** reliable results; however, they often come with significant drawbacks, including high resource consumption, waste generation, and potential hazards to both health and the environment.

New Synthetic Strategies

- **They** are emerging synthetic approaches leverage modern technology to enhance efficiency and safety.
- **These** strategies are with environmental sustainability, utilizing less harmful reagents and minimizing waste, thus addressing the ecological concerns associated with traditional methods.

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“Thank You”