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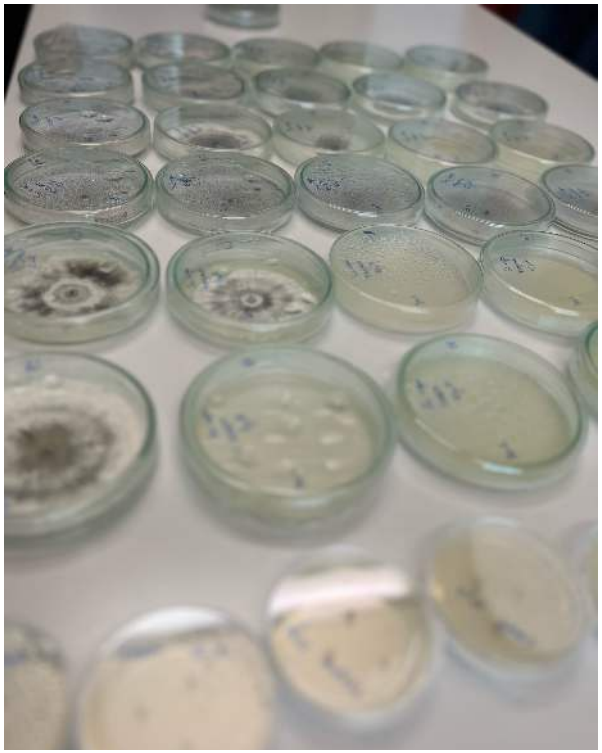
Cooperation to Implement Innovative Methods for the Assessment of Medicinal Plants with Central Roles in Pharmaceutics, Agriculture and Nutrition

ERASMUS KA220-HED - Cooperation partnerships in higher education

Project no. 2022-1-RO01-KA220-HED-000088958



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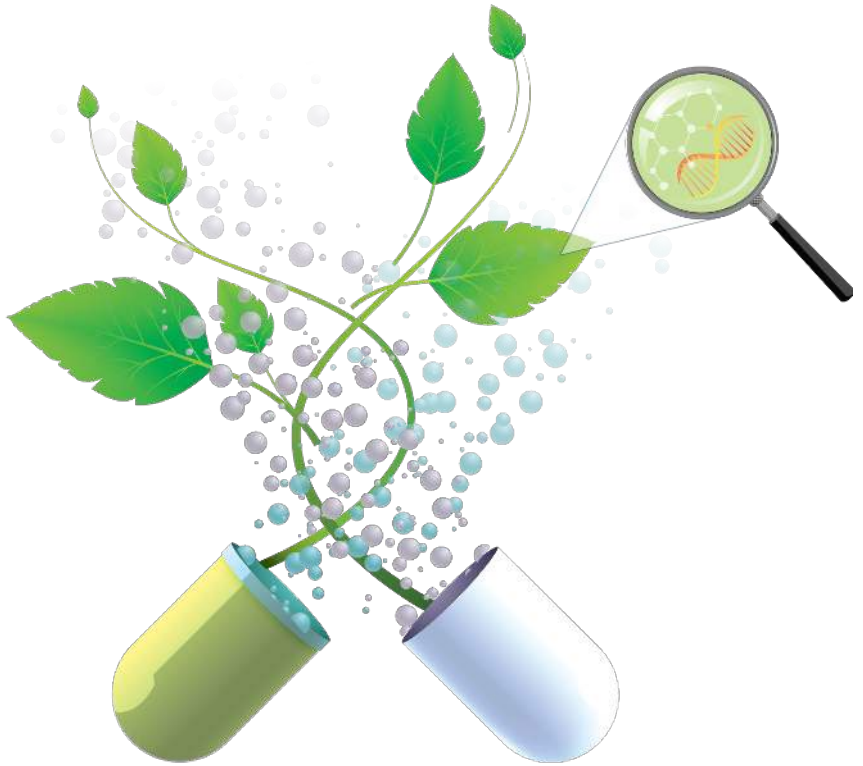
Aspects Related to the Safety of the Use of Medicinal Plants



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Overview

Why Medicinal Plants?

Used for centuries across cultures

Natural alternative to pharmaceuticals

Importance of Safety

Misuse can lead to adverse effects

Interaction with conventional medicines

Lack of regulation in some cases

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Types of Risks Associated with Medicinal Plants

Toxicity

- Some plants contain harmful compounds (e.g., aconitine in aconite)

Contamination

- Pesticides, heavy metals, or microbial contamination

Incorrect Identification

- Risk of using the wrong plant species

Allergic Reactions

- Some individuals may develop sensitivities

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Factors Affecting Safety

Dosage	Preparation Method	Duration of Use	Individual Differences
• Excessive intake can be toxic (e.g., ephedra causing heart issues)	• Boiling vs. raw consumption can change chemical composition	• Long-term use may lead to accumulation of toxic compounds	• Age, pregnancy, pre-existing health conditions

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Interaction with Conventional Medicines

Potential Interactions

- St. John's Wort reduces efficacy of antidepressants
- Ginkgo biloba increases bleeding risk when combined with blood thinners

Impact on Pharmacokinetics

- Medicinal plants can alter absorption, metabolism, and elimination of drugs

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Regulatory Challenges

Lack of Standardization

- Variability in active ingredient concentrations

Quality Assurance Issues

- Absence of strict manufacturing protocols

Limited Research

- Inadequate clinical trials compared to pharmaceuticals

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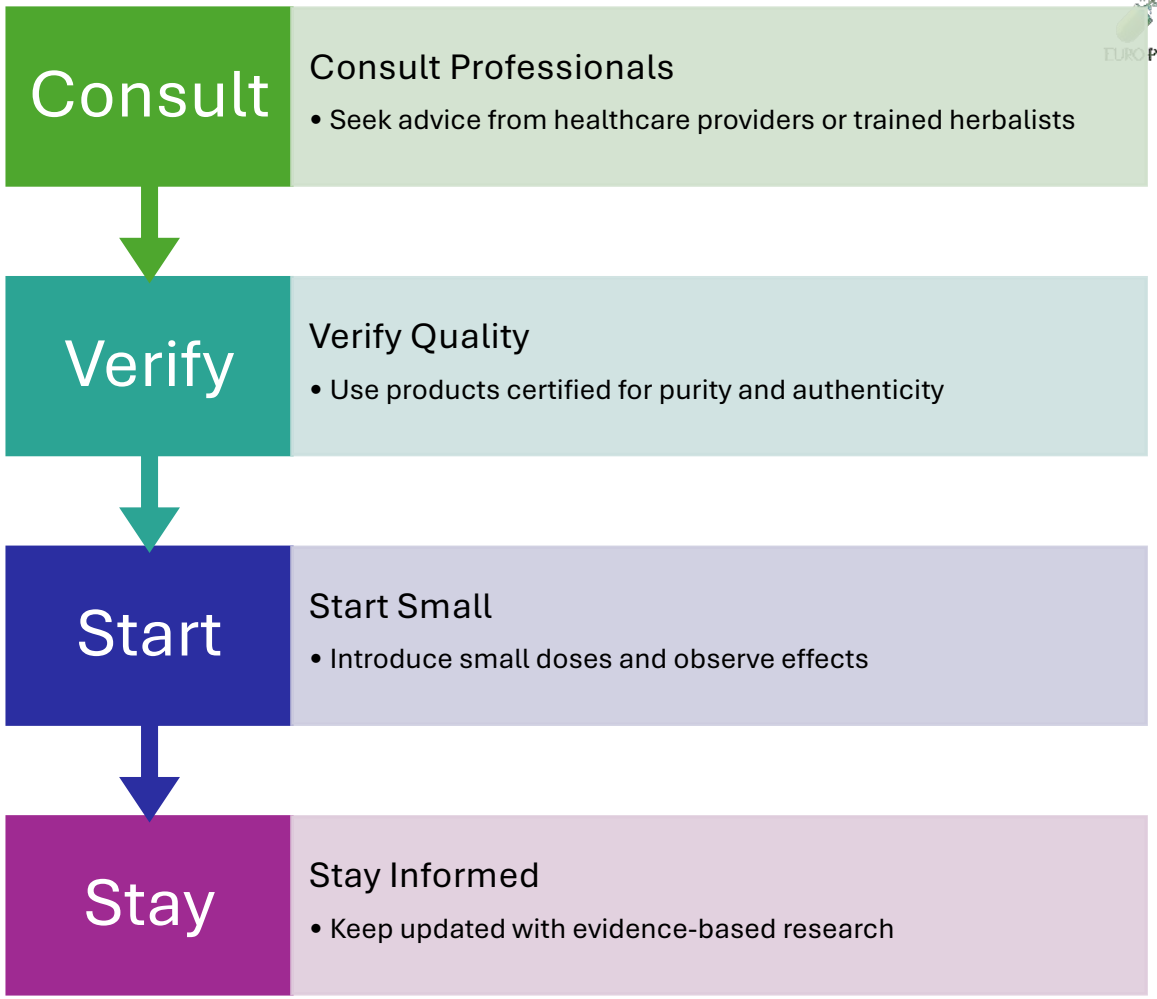
Recommendations for Safe Use



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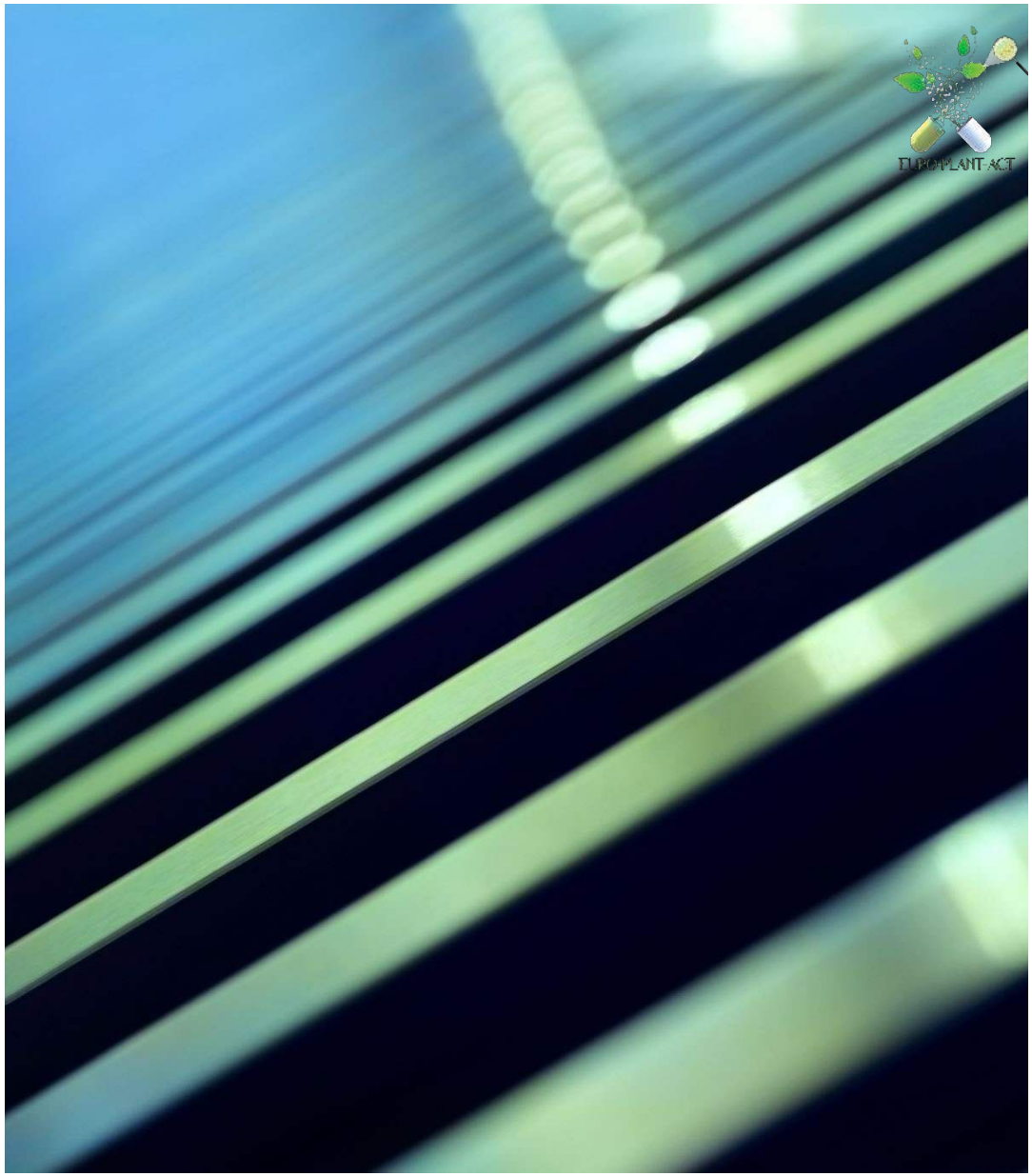
Case Studies

Positive Example: Aloe Vera

- Effective for minor burns and wounds when used topically

Negative Example: Aristolochia

- Linked to kidney failure and cancer due to toxic compounds



Role of Education and Awareness

- **Empowering Users**
  - Importance of understanding potential risks
- **Promoting Research**
  - Need for more studies on safety and efficacy
- **Advocating Regulation**
  - Encouraging governments to enforce stricter controls

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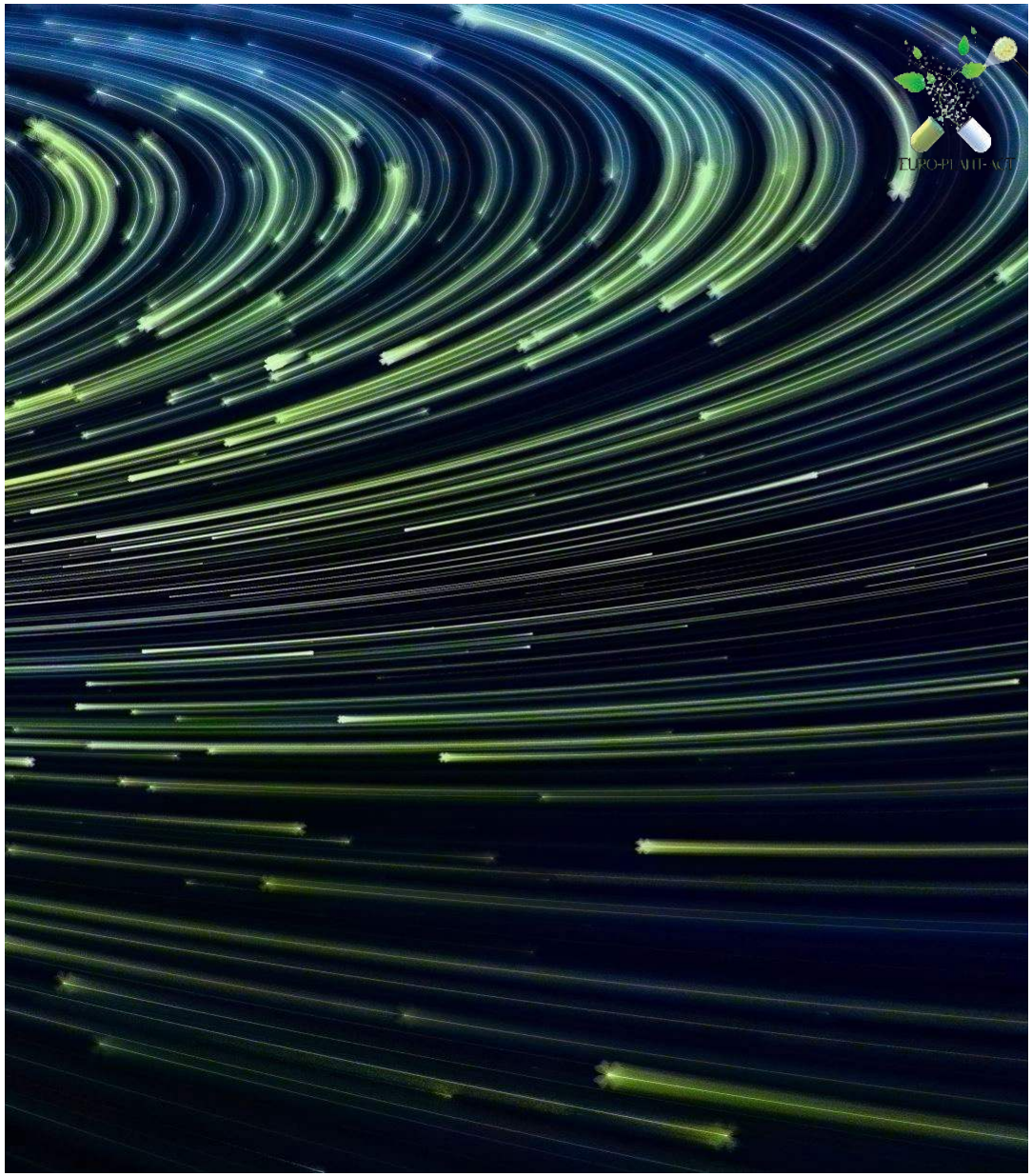
Conclusion

Key Takeaways

- Medicinal plants can be both beneficial and harmful
- Safety depends on informed use, proper dosage, and quality assurance
- Collaboration between traditional and modern medicine is essential

Final Thought

- "Natural" does not always mean "safe"—use with caution and knowledge.



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Presentation of the in vitro evaluation methods of biologically active compounds of interest in tumor pathologies

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Overview

Why In Vitro Evaluation?

- Rapid and cost-effective way to assess biological activity
- Provides insights into mechanisms of action

Applications in Tumor Pathologies

- Identifying potential anticancer agents
- Understanding cellular and molecular effects on cancer cells

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Key Objectives of In Vitro Testing

Primary Goals:

- Evaluate cytotoxicity against tumor cells
- Determine mechanisms of action (e.g., apoptosis induction)
- Assess selectivity between cancerous and normal cells

Advantages:

- High-throughput screening potential
- Controlled experimental environment

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Common Cell-Based Assays

Cytotoxicity Assays MTT/XTT/Resazurin Assays:

- Measure metabolic activity as an indicator of cell viability.

Trypan Blue Exclusion Test:

- Determines membrane integrity.

Proliferation Assays BrdU Incorporation:

- Detects DNA synthesis.

Colony Formation Assays:

- Measures the ability of single cells to form colonies.

Apoptosis Detection Flow Cytometry (Annexin V/PI):

- Quantifies apoptotic and necrotic cells.

Caspase Activity Assays:

- Identifies activation of caspase enzymes.

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Mechanistic Studies

1. Cell Cycle Analysis

- Flow cytometry using DNA-binding dyes (e.g., propidium iodide).

2. Gene and Protein Expression RT-PCR and Western Blotting:

- Evaluate expression of tumor-related genes/proteins.

Immunocytochemistry:

- Visualizes protein localization.

3. Intracellular Pathway Analysis

- Detect activation/inhibition of signaling pathways (e.g., PI3K/AKT, MAPK).

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Specialized In Vitro Models

1. 3D Cell Culture	Mimics tumor microenvironment better than 2D cultures. Examples: Spheroids, organoids.
2. Co-Culture Systems	Include cancer cells, stromal cells, and immune cells. Used to study tumor-immune interactions.
3. High-Content Screening	Combines automated microscopy with image analysis for multiparametric evaluation.

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Assays for Invasion and Metastasis

1. Migration Assays

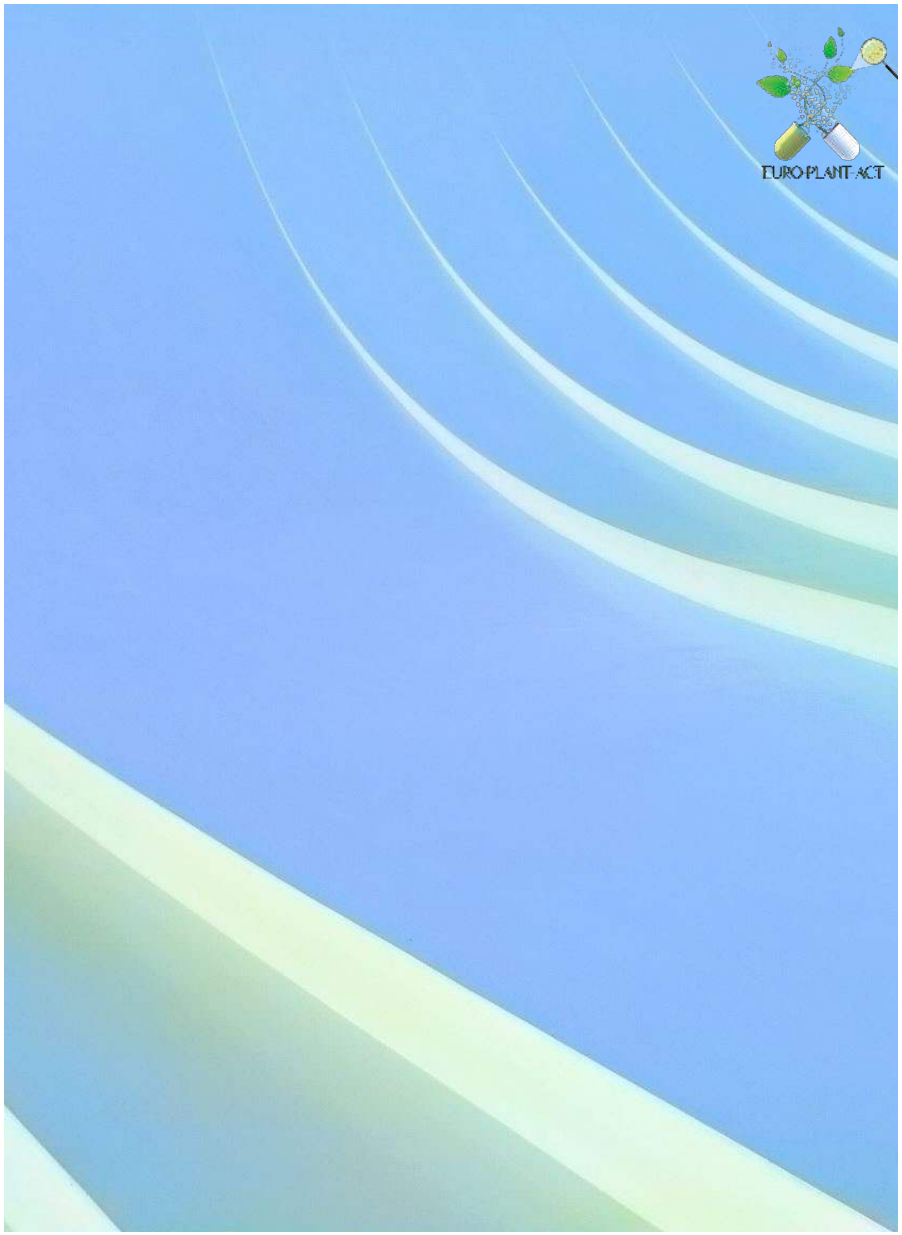
- Wound Healing/Scratch Assay: Measures cell migration into a cleared area.
- Transwell Migration Assay: Quantifies cell movement through membranes.

2. Invasion Assays

- Transwell with Matrigel: Mimics extracellular matrix for invasive capacity testing.

3. Angiogenesis Assays

- Tube Formation Assay: Evaluates the ability to form capillary-like structures.



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Evaluating Drug Resistance

1. Multidrug Resistance (MDR) Studies

Use of resistant cell lines to assess compound efficacy.

2. Efflux Transporter Assays

Evaluate the role of P-glycoprotein and other efflux mechanisms.

3. Synergy Testing

Combination Index Analysis (e.g., Chou-Talalay): Determines synergistic, additive, or antagonistic effects with other drugs.

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Limitations of In Vitro Models

Simplistic Nature

- Cannot fully replicate in vivo tumor complexity.

Lack of Immune System Representation

- Limited ability to assess immune-modulating effects.

Variability

- Differences in cell line behavior compared to primary tumors.

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Advancements and Future Directions

1. Organoid Cultures

- Patient-derived models for personalized testing.

2. Microfluidic Systems

- Lab-on-a-chip technology for simulating tumor microenvironment.

3. Artificial Intelligence

- Predicting compound efficacy based on in vitro data.

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Conclusions

Key Points:

- In vitro methods are essential for initial screening of anticancer compounds.
- A combination of assays provides a comprehensive evaluation.
- Advances in 3D models and personalized approaches are bridging gaps to clinical relevance.

Final Thought:

- Integration of innovative in vitro techniques with in vivo studies is key to developing effective anticancer therapies.

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Presentation of the in silico evaluation methods of biologically active compounds of interest in tumor pathologies

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Overview

Why In Silico Evaluation?

- Accelerates drug discovery by predicting biological activity
- Reduces cost and time compared to in vitro and in vivo studies

Applications in Tumor Pathologies

- Identifying potential anticancer agents
- Understanding molecular interactions and mechanisms

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Objectives of In Silico Methods

Primary Goals:

- Screen large libraries of compounds efficiently
- Predict binding affinity and biological activity
- Model tumor-related molecular mechanisms

Advantages:

- Non-invasive and resource-efficient
- Allows hypothesis generation for targeted experimentation

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Key In Silico Techniques

1. Molecular Docking

- Simulates binding interactions between small molecules and target proteins.
- Example tools: AutoDock, Glide.

2. Quantitative Structure-Activity Relationship (QSAR)

- Correlates molecular features with biological activity.
- Example tools: QSAR Toolbox, KNIME.

3. Molecular Dynamics (MD) Simulations

- Studies stability and behavior of drug-target complexes over time.
- Example tools: GROMACS, AMBER.

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Molecular Docking in Detail

Steps:

- Identify target protein (e.g., oncogenes, kinases).
- Use ligand libraries to find potential binders.
- Analyze docking scores and binding poses.

Applications in Tumor Pathologies:

- EGFR inhibitors in lung cancer
- BCL-2 inhibitors in leukemia

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QSAR Models

Overview:

- Uses statistical or machine learning models to predict activity.

Key Features:

- Molecular descriptors: lipophilicity, hydrogen bond donors/acceptors.
- Machine learning tools: Support Vector Machines, Random Forest.

Applications:

- Designing new molecules with enhanced selectivity for tumor cells.

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Molecular Dynamics Simulations

- **Purpose:**
  - Validate docking results by simulating real-time drug-target interactions.
- **Parameters Studied:**
  - Binding stability
  - Conformational changes
- **Applications:**
  - Understanding resistance mutations in cancer targets (e.g., T790M in EGFR).

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Virtual Screening

1. Ligand-Based Screening	Identifies similar molecules to known active compounds. Example: Searching for analogs of Taxol.
2. Structure-Based Screening	Uses 3D structure of the target protein to screen compounds. Example: Targeting VEGFR for anti-angiogenesis.

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Omics Integration

1. Genomics and Proteomics

- Identifying cancer-specific targets for personalized medicine.

2. Network Pharmacology

- Maps interactions between drugs, targets, and signaling pathways.

3. Databases and Tools

- DrugBank, PubChem, Cancer Cell Line Encyclopedia (CCLE).

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Predictive Toxicology

In Silico ADMET Modeling

- Predict Absorption, Distribution, Metabolism, Excretion, and Toxicity profiles.

Examples:

- Predicting hepatotoxicity or cardiotoxicity of anticancer agents.

Tools:

- pkCSM, SwissADME.

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Advantages and Limitations

Advantages:

- Saves time and resources in early drug discovery.
- Enables exploration of large chemical libraries.

Limitations:

- Relies on accuracy of computational models.
- May require experimental validation.

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Future Directions

1. AI and Machine Learning Integration

- Enhance predictive accuracy for drug discovery.

2. Big Data Analytics

- Utilize genomic and proteomic data for target identification.

3. Quantum Computing

- Revolutionizing molecular simulations for higher precision.

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Conclusions

Key Takeaways:

- In silico methods are indispensable in modern cancer research.
- Combine computational techniques with experimental validation.
- Continual advancements are driving personalized and effective therapies.

Final Thought:

- Computational tools are paving the way for next-generation cancer treatments.