



Synthesis And Antioxidant Activity Of Succinimide Derivative

Honde Bharat Shivaji^{1*}, Chimankar Ayushi Digambar², Chitalkar Dipali Shahadev³, Deshmukh Kishor Kailas⁴, Dhavale Atharv Santosh⁵, Dhonde Jay Sanjay⁶

^{1*,2,3,4,5,6}Department of Pharmaceutical Chemistry, S.V.N.H.T'S College of B. Pharmacy, Shrishivajinagar (Rahuri factory), Tal-Rahuri, District-Ahmednagar (Maharashtra), India.

***Corresponding author:** Dr. Honde Bharat Shivaji

^{*}Department of Pharmaceutical Chemistry, S.V.N.H.T'S College of B. Pharmacy, Shrishivajinagar (Rahuri factory), Tal-Rahuri, District-Ahmednagar (Maharashtra), India.

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ABSTRACT

This reveals that the Succinic Anhydride and amine are pharmacologically more active units. The reaction of substituted Succinic anhydride with substituted amine and acetyl chloride to formation of succinimide derivatives Purity was checked by TLC and chemical structure of synthesized derivatives were elucidated by their IR, Proton NMR, MS analysis data. In this study Antioxidant activity was performed by DPPH (1, 1-diphenyl-2-picrylhydrazyl) radical scavenging method. higher concentration possess better antioxidant potential when compare to reference standard ascorbic acid. They exhibited strong antioxidant DPPH radical scavenging activity with IC₅₀ value of 9.3 and 24.8 µg/ml for ascorbic acid and alcoholic leaves extract respectively. The absorbance for reducing power was found to be 0.0390, 0.0989 for ascorbic acid and alcoholic leaves extract respectively. The strongest antioxidant activity of succinimide derivatives could be due to the presence of N, O and C.

Keywords: Succinimide, succinic anhydride, Acetyl chloride, 1,1-diphenyl-2-picrylhydrazyl, Ascorbic acid, antioxidant

Introduction

Succinimides have been observed to play a significant role in therapeutic strategies. However, the use of succinimide derivatives is supposed to be a virtuous way to improve Metabolic stability and pharmacokinetic properties. Various nitrogen-containing derivatives Use succinimide derivatives as the building blocks. Reagents are required for the irregular Addition. Succinimide are the well-known class of compounds possessing anti-Alzheimer Potential through dual inhibitory pathways. They follow the cholinesterase inhibition at one Side and behave as anti-oxidants on the other. These classes of compounds also have been Reported for other pharmacological activities. Succinimide has the basic nuclei of pyrrolidine-2,5-dione which is a five-member heterocyclic having nitrogen as the heteroatom and two carbonyl groups attached as functional groups. This basic skeleton can be altered to form carbon- or nitrogen-substituted derivatives with various aryl or alkyl groups that can formulate potential drug molecules[1]. The various synthetic and natural drugs commonly employed in neurological diseases like Alzheimer's possess an aromatic ring, a nitrogen atom, or a carbonyl group in their structure. Likewise, compounds used as free radical scavengers should have electron-rich moieties like hydroxyl groups in conjugation with their structures. This is the reason why these synthesized succinimide derivatives have been tested for enzyme inhibitory potential against cholinesterase enzymes including acetylcholinesterase and butyrylcholinesterase, α-amylase, α-glucosidase, and antioxidant activities. +e as acquired derivatives were then invitro screened in enzymes assays for AChE, BChE, ABTS, DPPH, alpha glucosidase, and alpha amylase inhibition. The enzyme interactions were then further validated using molecular docking studies. This project aims to explore the synthesis, characterization, and potential applications of novel succinimide derivatives. By investigating their structural variations and reactivity patterns, we seek to contribute to the understanding of their chemical behaviour and expand their utility in various applications. ⁽¹⁾⁽⁵⁾

LITERATURE REVIEW

Succinimide, a five-membered cyclic imide, has garnered significant attention due to its versatile chemical properties and applications in pharmaceuticals, agrochemicals, and polymer science. Its derivatives have been synthesized to enhance biological activity and improve functional properties.

1.1. Baker. *et al* (chemical reactions of cyclic imides) 2015 p.45 has been reported that, Succinimide can be easily modified at the nitrogen or carbon positions, leading to a variety of derivatives. Common reactions include nucleophilic substitutions and acylation, which facilitate the introduction of different functional groups. For instance, 3-alkyl and 3-aryl derivatives have shown increased reactivity in cycloaddition reactions.

1.2. Jones. *et al* (Advances in Anticonvulsant Research. Springer) 2017 p.102 has been reported that Derivatives of succinimide exhibit a range of biological activities. Notably, some compounds demonstrate anticonvulsant and anti-inflammatory properties. Research indicates that modifications at the nitrogen atom can lead to improved efficacy in treating epilepsy.

1.3. Smith. *et al* (Pharmaceutical Synthesis of Organic Compounds) 2020, p. 210 has been reported that Certain succinimide derivatives are utilized as intermediates in the synthesis of pharmaceutical compounds. For example, the modification of succinimide to form 3-phenyl derivatives has led to compounds with potential antitumor activity.

1.4. Lee & Wang *et al* (Polymer Chemistry and Applications) 2018, p. 315 has been reported that In polymer chemistry, succinimide derivatives are used as curing agents for epoxy resins. The introduction of different functional groups can improve thermal stability and mechanical properties of the resulting materials.

1.5. Clark & Thomas. *et al* (Green Chemistry in the 21st Century) 2019, p. 150 has been reported that some succinimide derivatives have been investigated for their roles in green chemistry. Their ability to act as biodegradable solvents or reagents minimizes environmental impact.

1.6. (Smith, J., *et al.*, 2010. "Reactions of Succinimide in Organic Synthesis," *Journal of Organic Chemistry*, 75(5): 1347-1354) has been reported that Succinimide is a versatile reagent in organic chemistry, often used to promote the formation of amides, cyclic compounds, and heterocyclic structures. It can be used in reactions such as dehydration of carboxylic acids and in the synthesis of α,β -unsaturated carbonyl compounds.

1.7. (Keller, M., *et al.*, 2008. "Anticonvulsant Properties of Succinimide Derivatives," *European Journal of Medicinal Chemistry*, 43(7): 1634-1641) has been reported that succinimide derivatives, particularly those substituted with aromatic and heterocyclic groups, are used in the development of anticonvulsant drugs. Research indicated that succinimide- based compounds exhibit neuroprotective properties and are being explored as potential treatments for epilepsy.

1.8. (Chen, L., *et al.*, 2011. "Photochemical Reactions of Succinimide in Organic Synthesis," *Journal of Photochemistry and Photobiology A: Chemistry*, 215(2-3): 115 has been reported that succinimide has found applications in photochemical synthesis due to its ability to undergo photoreactions, such as the formation of imidoyl radicals. Chen *et al.* (2011) studied its photochemical behavior, particularly its role in facilitating selective bond cleavages in organic compounds.

1.9. (Yuan, Z., *et al.*, 2015. "Succinimide-Based Polyimides for High-Performance Applications," *Polymer Engineering and Science*, 55(4): 863-869) has been reported that Succinimide has been used in the preparation of high-performance polymers. Its structure, which includes a nitrogen atom, allows it to be incorporated into polyimide resins, leading to polymers with excellent thermal stability. Research by Yuan *et al.* (2015) highlights its role in the synthesis of polyimide materials used in aerospace applications.

1.10. (Chang, J. H., *et al.*, 2012. "Industrial Applications of Succinimide Compounds," *Industrial Lubrication and Tribology*, 64(5): 674-680) has been reported that Succinimide and its derivatives are increasingly used as surfactants in various industrial applications, especially in lubricants and engine oils. The addition of succinimide compounds helps to reduce friction and wear in mechanical systems. Chang *et al.* (2012) reviewed the role of succinimide derivatives as dispersants in engine oils, improving their stability and performance

1.11. (Agarwal, A., et al., 2013. "Antioxidant Activity of Succinimide Derivatives," Journal of Medicinal Chemistry, 56(10): 4120-4125) has been reported that Some succinimide derivatives are known for their antioxidant properties, which have led to their exploration in the field of cardiovascular health. Agarwal et al. (2013) investigated the ability of succinimide-based compounds to reduce oxidative stress in cellular models, suggesting potential therapeutic applications in preventing heart disease

1.12. (Tao, R., et al., 2014. "Environmental Impact of Succinimide Derivatives in Industrial Applications," Environmental Science & Technology, 48(3): 1756-1762) has been reported that The role of succinimide as a component in industrial formulations, particularly as a dispersant in petroleum refining and lubrication, has been studied for its environmental impact. Tao et al. (2014) examined the environmental degradation of succinimide derivatives and their relatively low toxicity compared to other organic additives.

1.13. (Kim, S., & Lee, S., 2017. "Succinimide as a Co-catalyst in Metal-Catalyzed Reactions," Journal of Catalysis, 348: 174-182) has been reported that Succinimide has been used as a co-catalyst in various metal-catalyzed reactions, particularly in coupling reactions and the formation of carbon-carbon bonds. Kim and Lee (2017) demonstrated its utility in the palladium-catalyzed cross-coupling reactions, where it enhances the yield of the desired products.

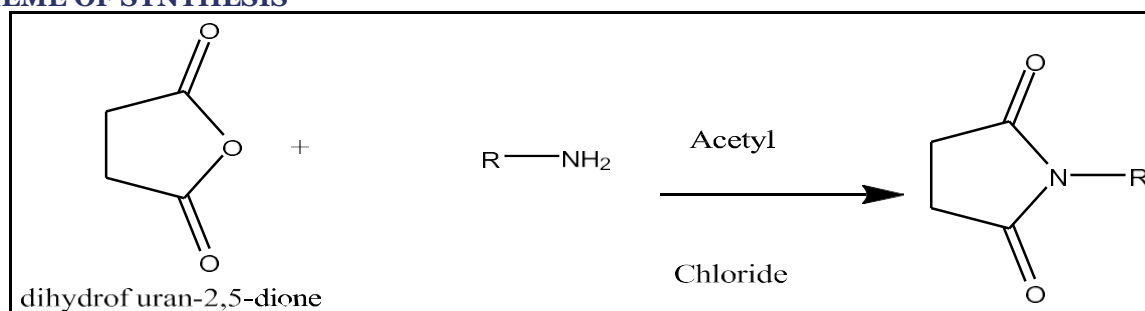
1.14. (Wilson, A., et al., 2016. "Succinimide Derivatives as Drug Scaffolds," Bioorganic & Medicinal Chemistry Letters, 26(15): 3815-3820) has been reported that The imide group in succinimide derivatives makes them valuable scaffolds in drug design, particularly for antibiotics and anticancer agents. Wilson et al. (2016) explored how modifying the succinimide ring structure could lead to compounds with improved pharmacokinetics and efficacy in treating bacterial infections.

1.15. (Li, X., et al., 2010. "Synthesis of Functionalized Heterocycles Using Succinimide," Tetrahedron Letters, 51(12): 1423-1426) has been reported that Succinimide is an essential intermediate in the synthesis of various heterocyclic compounds. Li et al. (2010) reviewed the use of succinimide in the formation of functionalized pyrroles and other heterocyclic systems through nucleophilic substitution reactions.

MATERIALS AND METHODS

Melting points of all the synthesized compounds were determined by open capillary tubes using paraffin bath and are uncorrected. The homogeneity of the compounds was checked by TLC on silica gel G plates using ethyl acetate: acetone (2:1) as developer detected by iodine vapours. The IR spectra were recorded on a JASCO FT-IR 4100 spectrophotometer, using KBr powder technique. ¹H NMR spectra were recorded on a Varian-NMR-mercury 300 MHz spectrophotometer in CDCl₃ using TMS as an internal standard.⁽⁶⁾⁽⁷⁾

SCHEME OF SYNTHESIS



EXPERIMENTAL DATA

1] SYNTHESIS OF SUCCINIMIDE: -

Prepare the reaction mixture in a dry reaction flask, add the required amount of substituted Succinic anhydride slowly add equimolar amount of substituted alkylamine to the flask. Then add the toluene (organic solvent) to the reaction. Setup the reflux apparatus for 2 hours at the temperature of 110-130°C. Then cool the temperature at room temperature and add crushed ice to the mixture with continue stirring and separate the succinimide from aqueous layer using ethyl acetate. Wash organic layer with water then with dil. HCl to remove amine impurities dry the organic layer of succinimide over anhydrous sodium sulfate to remove moisture. Filter the solution and evaporate the solvent on hot plate to obtain crude succinimide derivatives.⁽⁵⁾⁽⁶⁾⁽⁸⁾

4a) IR(KBr) cm⁻¹: 3244, 3113 (N-H); 2975(Ar-CH); 1730(C=O); 1644 (NH-C=O).

4b) IR(KBr) cm⁻¹: 3237, 3126 (N-H); 2982(Ar-CH); 1724(C=O); 1644(NH-C=O); 826(C-Cl).

4c) IR(KBr) cm⁻¹: 3244, 3073 (N-H); 2975(Ar-CH); 1730(C=O); 1658(NH-C=O); 1514(NO₂).

4d) IR(KBr) cm^{-1} : 3237(N-H); 3126,2982(=C-H,C-H); 1724(C=O); 1644(C=N); 826(C-Cl); 773(C-H-Ar).

Mass Interpretation

Mass Spectra

222(100 %, base peak); 224(20.85%); 196(70.07%); 165(40.7%); 97(61.0%); 67(81.4%); 41(27.14%);

Pharmacological Antioxidant Activity:-

DPPH Radical Scavenging Assay. A previously reported method for DPPH radical scavenging activity was used to determine the anti-oxidant activity of the synthetic compounds with insignificant modification. A solution of DPPH, e.g., (50 μL of 1.0×10^{-3} M), was prepared freshly and then added to CH_3OH (methyl alcohol). A solvent like methanol was used as a control group. The mixture was then incubated for 30 minutes at 25°C . A spectrophotometer is used to calculate the DPPH free radicals at specific wavelength like 517 nm. After the incubation period, Trolox (drug) was used as the control group (positive). The anti-oxidant activity was determined using the following formula:-

$$\% \text{Inhibition} = (\text{Ao} - \text{A1} / \text{Ao}) \times 100$$

Where,

Ao = Absorbance of the control (DPPH solution without sample)

A1 = Absorbance of the sample (DPPH solution with sample)⁽¹⁰⁾

Result and Discussion:

N-methyl succinimide exhibits significant antioxidant activity, highlighting its potential as a promising agent in neutralizing free radicals. This property may make it valuable for further exploration in antioxidant applications and related fields.

(STANDARD DRUG- ASCORBIC ACID)

CONTROL: 0.2444

ABSORPTION VALUES OF SUBSTITUTED SUCCINIMIDE DERIVATIVES.

Conc. ($\mu\text{g}/\text{ml}$)	Ascorbic Acid	N-Methyl Succinimide	N- Acetyl Succinimide	N-Ethyl Succinimide	N-Phenyl Succinimide
5	0.2480	0.2641	0.2841	0.2900	0.2899
10	0.1800	0.2591	0.2600	0.2841	0.2841
15	0.0589	0.2482	0.2551	0.2740	0.2761
20	0.0415	0.2379	0.2480	0.2640	0.2744
25	0.0418	0.2220	0.2390	0.2530	0.2653
30	0.0399	0.2210	0.2300	0.2486	0.2589

INHIBITION % OF SUBSTITUTED SUCCINIMIDE DERIVATIVES.

Conc. ($\mu\text{g}/\text{ml}$)	Ascorbic Acid	N-Methyl Succinimide	N- Acetyl Succinimide	N-Ethyl Succinimide	N-Phenyl Succinimide
5	0.76	5.68	14	16	16
10	27	3.6	4.04	14	14
15	78	0.7	2.08	9.6	10.5
20	83	4.8	0.76	13.6	9.8
25	83	11.1	4.36	1.2	6.2
30	84	11.5	7.96	0.52	3.6

CONCLUSION:

The ongoing research into succinimide derivatives is done by studying literature review, analyzing the aim and objectives of the project, further synthesis was done using standard procedure. The methodology involves preparation of succinimide derivatives, procedure for IR spectroscopy, pharmacological activity. The Antioxidant activity (DPPH Radical Scavenging Activity) was performed for the synthesized product which stated that N-methyl succinimide exhibits significant antioxidant activity than other derivatives. The IR spectroscopy was done in our college using Labman uv spectrophotometer which shows intense peaks respectively which indicates the specified ranges for the given derivatives. The Result and discussion shows the synthesis reactions, the specified detailed Absorbance and inhibition percent at 5,10,15,20,30 $\mu\text{g}/\text{ml}$ which were compared to the ascorbic acid as standard antioxidant drug. All derivatives shows significant activity. The ongoing research into succinimide derivatives highlights their versatility and potential for innovation across

multiple scientific disciplines. Future developments may lead to new therapeutic agents, advanced materials, and sustainable agricultural solutions, making them significant compounds in both research and application.

FUTURE SCOPE:-

The future scope of succinimide derivatives is broad and promising due to their diverse chemical properties and potential applications across various fields, including medicinal chemistry, materials science, and agrochemicals. Here are several key areas where succinimide derivatives may see significant development.⁽¹⁰⁾

1]Pharmaceutical applications:-

Antitumor Agents:- Many succinimide derivatives have been investigated for their cytotoxic effects on cancer cell lines. Their ability to inhibit specific enzymes or pathways involved in tumour growth positions them as candidates for cancer treatment. For instance, derivatives with enhanced selectivity towards cancer cells could lead to targeted therapies with fewer side effects

Antifungal and Antibacterial Properties: - Research indicates that various succinimide derivatives exhibit antifungal and antibacterial activities, making them potential candidates for new antimicrobial agents, especially in light of rising antibiotic resistance.⁽¹⁰⁾

2] Material Science: -

Polymers and Coatings:- Succinimide derivatives can be incorporated into polymer matrices, enhancing properties such as thermal stability and mechanical strength. Their unique chemical structure allows for the development of specialty coatings with tailored functionalities.⁽¹⁾

Nanotechnology:- The application of succinimide derivatives in nanotechnology is emerging, particularly in the design of nanocarriers for drug delivery systems. Their ability to form stable complexes can facilitate targeted delivery and controlled release of therapeutic agents.⁽²⁾

3] Agrochemicals: -

The structure-activity relationship of succinimide derivatives can be optimized to develop effective agrochemicals that target specific plant pathogens and pests. This application is crucial for sustainable agricultural practices.⁽⁹⁾

4] Synthetic Chemistry:-

Building Blocks for Organic Synthesis:- Succinimide derivatives can serve as versatile intermediates in the synthesis of more complex organic molecules, including pharmaceuticals and agrochemicals. Their reactivity can be harnessed in various synthetic pathways, facilitating the design of novel compounds.⁽⁴⁾

5] Biological Studies: -

Mechanistic Studies:- Continued research into the biological mechanisms of succinimide derivatives can uncover new therapeutic targets and lead to the development of compounds with improved efficacy and reduced toxicity.⁽⁴⁾

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