Antioxidant activity of synthesized (*E*)-*N*-(2-(1*H*-indol-3-yl-amino) vinyl)-3-(1-methyl-1*H*-indol-3-yl)-3-phenylpropanamide derivatives 3(a-e)

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Abstract

The synthesized (*E*)-*N*-(2-(1*H*-indol-3-ylamino) vinyl)-3-(1-methyl-1*H*-indol-3-yl)-3-phenyl propanamide derivatives 3(a-e) were subjected to allowed for *in vitro*antioxidant activityby adopting DPPH• scavenging method and the absorbance is measured at 517 nm range. The *In vitro* Antioxidant activity results showed that compounds 3e, 3c, 3b and 3d had good antioxidant potency, 3a had moderate activity, the encouraging results exhibited by the title compounds 3(a-e).

Introduction

Indole derivatives being biodynamic heterocycles and possess wide range of importance in pharmaceutical applications. Literature reveals that many indole derivatives were reported to possess antimicrobial potential in several studies, among them ethyl-3-indolylacrylate, 5-bromo-3-(2-cyanovinyl) indole and 3-(2-nitrovinyl)-indole and indolecarboxamides were found to be active against a wide variety of pathogenic microorganisms [1, 2].

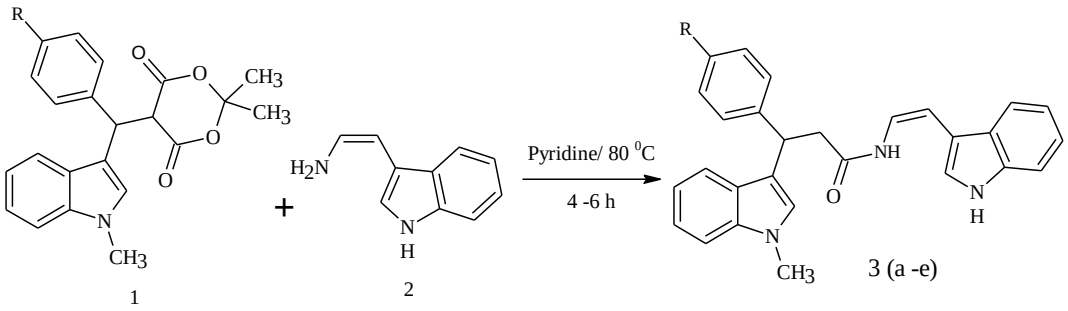
The halo substituted indole derivatives were found to be highly active [3], some other indole derivatives such as, 3-acyl-4, 7-dihydroxy indole possess antibacterial properties against *Escherichia coli* and *Streptococcus pyogenes*[4]. 1-morpholino-3-carbethoxy-5-hydroxy-2-methylindole was reported to be highly active against *Escherichia coli* and *Bacillus cirroflagellosu*[5] and 1-(4-phenyl) and (1-naphthyl-4*H*-1, 2, 4-triazole-5-thion-3-yl) indole also exhibited strong antibacterial and antifungal activities [6]. Survey revealed that N-H and *N*-substituted indole-3-propanamide derivatives reported as antioxidant agents, antimicrobial, antifungal and anti-HBV activities [6, 7]. Indole-3-propanamide derivatives do possess immunosuppressive potential. Synthetic derivatives, 3-[1-(4-chlorobenzyl) indol-3-yl]-N-(pyridin-4-yl) propanamide (AD412) possessed strong immunosuppressive potential, **a**nd

3-[1-(4-chlorobenzyl)-1*H*-indol-3-yl]-*N*-(pyridin-4-yl)propanamide compounds [8] inhibited, the proliferative response to IL-2. The compounds exert its immunosuppressive activity by inhibiting IL-2-induced JAK3 activation.The synthesized (1*H*-indol-3-yl)alkyl-3-(1*H*-indol-3-yl)propanamide was evaluated by Karuvalam*et. al.,*2013 [8]; for their preliminary *in vitro* antimicrobial, antifungal and also screened for their antitubercular activity against *mycobacterium tuberculosis* H37Rv strain[9].

Rationality

Indole is known to possess fundamental tenets for various organic intermediates as well as synthetic drug molecules. They had wide range of biological activities as we discussed in introduction part [1-7]. The rationality in investigating the biopotency of indole-3-propanamide derivatives is due to its use as precursors to obtain several biologically active molecules, especially for the treatment of brain disorder [9], as tyrosine kinase inhibitors, inhibitors of epidermal growth factor (EGF) receptor [10,11], immunosuppressive activity [12,13] anti-allergic [14] and inflammation inhibitors [15]. Thus, indole-3-propanamides have become an important precursor for various pharmaceutically important compounds [16-18] and there is flexibility in exploring indole-3-propanamide derivatives randomly for various biological activities to get suitable hits.

Synthesized scheme



R = H, Cl, NO_2, NH_2, Br

Synthesis of (*E*)-*N*-(2-(1*H*-indol-3-yl-amino) vinyl)-3-(1-methyl-1*H*-indol-3-yl)-3-phenylpropanamide derivatives 3(a-e)

Synthesis of (*E*)-*N*-(2-(1*H*-indol-3-ylamino) vinyl)-3-(1-methyl-1*H*-indol-3-yl)-3-phenyl propanamide derivatives (3a)

Various substituted meldrum's adducts [19] (4) (1 mol) and (*E*)-2-(1*H*-indol-3-yl) ethenamine2 (1 mol) were weighed and dissolved in 5 ml pyridine, kept for refluxed at 80 °Cabout 4-6 hrs. The progress of the reaction was monitored by using pre-coated silica gel TLCplates (Merck). After completion, the product was treated with copper sulphate solution and extracted from ethyl acetate, crude product was isolated and column purified by using silica (60-120)mesh, and mobile phase petroleum ether: ethyl acetate 9:1 v/v) to get the pure (*E*)-*N*-(2-(1*H*-indol-3-yl-amino) vinyl)-3-(1-methyl-1*H*-indol-3-yl)-3-phenylpropanamide (3a**)**. Similarly, the other derivatives3 (b-e) were prepared by adopting the standard procedure mentioned here.

Antioxidant Activity

DPPH• Scavenging Activity

DPPH is a stable free radical that can accept an electron or hydrogen radical to become a stable diamagnetic molecule. Due to its odd electron, the methanolic solution of DPPH shows a strong absorption band at 517 nm. DPPH radical reacts with various electron donating molecules (reducing agents or antioxidants). When electrons become paired off, bleaching of the DPPH solution is the result. This results in the formation of the colourless 2,2'-diphenyl-1-picryl hydrazine. Reduction of the DPPH radicals can be estimated quantitatively by measuring the decrease in absorbance at 517 nm.

Procedure: Equal volumes of 100 µm2,2'-diphenyl-1-picrylhydrazyl (DPPH) in methanol was added to different concentrations of test compounds (100 µm/ml) in methanol, mixed well and kept in dark for 20 min. The absorbance at 517 nm was measured using the spectrophotometer UV-1650, Shimadzu [20]. Plotting the percentage DPPH scavenging against concentration gave the standard curve and the percentage scavenging was calculated from the following equation:

$$\% \text{ scavenging} = \frac{\text{Absorbance of blank-Absorbance of test}}{\text{Absorbance of blank}} \times 100$$

Result and Discussion

The synthesized (*E*)-*N*-(2-(1*H*-indol-3-ylamino) vinyl)- 3-(1-methyl-1*H*-indol-3-yl)-3-phenylpropanamides 3(a-e) were allowed for *in vitro* antioxidant activity by DPPH method. The results from the activity were revealed that the compounds 3b, 3c, 3d and 3e having chlorine, bromine, nitro and amines groups, respectively on phenyl ring exhibit potent antioxidant activity.

Table 1: Results showed the antioxidant activity of (*E*)-*N*-(2-(1*H*-indol-3-ylamino) vinyl)- 3-(1-methyl-1*H*-indol-3-yl)-3-phenylpropanamides 3(a-e).

SI No	Sample code	Antioxidant Potential (mean±SD)
1	3a	29 ± 0.16
2	3b	38 ± 0.25
3	3c	40 ± 0.18
4	3d	37 ± 0.18
5	3e	44 ± 0.30
6	Ascorbic acid	98 ± 0.33

SD: standard deviation

Conclusion

The synthesized (*E*)-*N*-(2-(1*H*-indol-3-yl-amino) vinyl)-3-(1-methyl-1*H*-indol-3-yl)-3-phenylpropanamide derivatives 3(a-e), were found to be good *In vitro* antioxidant activity,

The antioxidant activity was envisaged by DPPH method, among the tested samples 3e, 3c had 44±0.30 and 40±0.18, respectively as compared with positive control Ascorbic acid. In concluding the antioxidant results of the synthesized compounds 3(a-e) were adequate to the potential to form hits/leads for future drug candidates.

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