INTRODUCTION

Oxidation is a chemical reaction characterized by transfer of an electron from electron rich to electron deficient entity. Antioxidant is a molecule that inhibits the oxidation of other molecules. Antioxidants are intimately involved in the prevention of cellular damage the common pathway for cancer, aging, and a variety of diseases. Antioxidants are widely used in dietary supplements and have been investigated for the prevention of diseases such as cancer, coronary heart disease and even altitude sickness. The wide occurrence of the heterocycles in bioactive natural products, pharmaceuticals, and agrochemicals has made them as important synthetic targets. Several five-membered heterocyclic drugs possess diverse biological effects. Nitrogen and oxygen containing five-membered azoles are important bioactive molecules, due to their wide array of pharmacological activities such as anti fungal, antimicrobial, anti-inflammatory, analgesic, hypolipidemic, anti tubercular, anti-convulsant and cytotoxic agents and anti oxidant agent.

Literature survey revealed that attachment of different pharmacophores to 1,3,4-oxadiazole lead to qualitative as well as quantitative changes in the biological activity. Prompted by the above findings we have studied antioxidant activity of synthesized 2-nonyl-5-ary1,3,4-oxadiazole derivatives by DPPH protocol.

MATERIALS AND METHODS

All the common solvents and chemicals were of LR grade and were procured from Central Drug House (CDH) Ltd, Merck India and Sigma Aldrich. The purity of the synthesized compounds was ascertained by by silica gel G coated TLC plate and the Rf values were determined. Melting points were determined by the capillary method. The infrared (IR) spectra were recorded on Perkin Elmer IR 4000-400 (in cm⁻¹) spectrophotometer and NMR spectra of synthesized compounds were recorded on Bruker Advance II 400 (400 MHz, ¹H NMR) instrument. Chemical shifts are reported as parts per million (ppm) using tetramethylsilane (TMS) as an internal standard.

Table 1: Characterization data of oxadiazole derivatives (3a-h)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Molecular formula</th>
<th>% yield</th>
<th>M.p. (°C)</th>
<th>Rf</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>C₁₃H₁₄N₂O</td>
<td>84</td>
<td>24</td>
<td>0.7</td>
</tr>
<tr>
<td>3b</td>
<td>C₁₃H₁₂ClN₂O</td>
<td>86.6</td>
<td>42</td>
<td>0.76</td>
</tr>
<tr>
<td>3c</td>
<td>C₁₃H₁₄N₂O</td>
<td>98</td>
<td>39</td>
<td>0.67</td>
</tr>
<tr>
<td>3d</td>
<td>C₁₃H₁₂F₂N₂O</td>
<td>96</td>
<td>28</td>
<td>0.57</td>
</tr>
<tr>
<td>3e</td>
<td>C₁₃H₁₂N₂O₂</td>
<td>89</td>
<td>29</td>
<td>0.67</td>
</tr>
<tr>
<td>3f</td>
<td>C₁₃H₁₂ClN₂O</td>
<td>82</td>
<td>40</td>
<td>0.60</td>
</tr>
<tr>
<td>3g</td>
<td>C₁₃H₁₂ClN₂O</td>
<td>80</td>
<td>45</td>
<td>0.57</td>
</tr>
<tr>
<td>3h</td>
<td>C₁₃H₁₂ClN₂O</td>
<td>85</td>
<td>50</td>
<td>0.61</td>
</tr>
</tbody>
</table>

Experimental

Procedure for synthesis of ester (1)
The esterification was carried out by using (0.1 Mol) of n-Capric acid in 32 ml of absolute ethanol and 1.1 ml of...
H₂SO₄ and refluxed for 5-6 h. Mixture was poured into separating funnel containing diethyl ether and ether layer extracted, dried under vacuum and used for further reaction.

Procedure for synthesis of acid hydrazide (2)

A mixture of ester 1 (0.1 mol) and hydrazine hydrate 99% (0.11 mol) in 50 ml absolute ethanol was reflux for 5-6 h. The reaction mixture was cooled and left overnight. Solid obtained was collected and recrystallized from absolute ethanol.

Procedure for synthesis of (3a-h)

An equimolar amount of compound 2 and appropriate aromatic acids in 10 ml phosphorus oxychloride (POCl₃) was refluxed for 5 h. The reaction mixture was cooled and stirred. The potassium hydroxide solution was added till the pH of the mixture raised to 8. The precipitate was filtered and recrystallized from absolute ethanol.

2-nonyl-5-phenyl-1,3,4-oxadiazole (3a)

IR (KBr), ν cm⁻¹: 2938 (C-H, Ar), 1596 (C=N), 1152 (C-O-C), 720 (C-Cl). ¹HNMR (CDCl₃) δ (ppm): 8.3 (m, 3H, Ar-H), 8.05-8.4 (m, 4H, Ar-H), 4.55-4.75 (s, 2H, CH₂).

2-(4-chlorophenyl)-5-nonyl-1,3,4-oxadiazole (3b)

IR (KBr), ν cm⁻¹: 2926 (C-H, Ar), 1601 (C=N), 1104 (C-O-C), 720 (C-Cl). ¹HNMR (CDCl₃) δ (ppm): 7.2-7.4 (m, 3H, Ar-H), 4.5-4.7 (s, 2H, CH₂).

2-(4-methoxyphenyl)-5-nonyl-1,3,4-oxadiazole (3c)

IR (KBr), ν cm⁻¹: 2935 (C-H, Ar), 1604 (C=N), 1103 (C-O-C), 1259, 1027 (-OCH₃). ¹HNMR (CDCl₃) δ (ppm): 6.9-7.03 (m, 3H, Ar-H), 7.2-7.4 (m, 4H, Ar-H), 4.5-4.7 (s, 2H, CH₂), 3.8-3.9 (s, 3H, CH₃).

2-(4-fluorophenyl)-5-nonyl-1,3,4-oxadiazole (3d)

IR (KBr), ν cm⁻¹: 2925 (C-H, Ar), 1592 (C=N), 1091 (C-O-C), 1032 (C-F). ¹HNMR (CDCl₃) δ (ppm): 7.2-7.4 (m, 4H, Ar-H), 4.2-4.5 (s, 3H, CH₃), 3.4-3.7 (s, 3H, CH₃), 2.1-2.9 (s, 6H, CH₂), 1.2-1.8 (s, 8H, CH₂) 0.8-0.9 (s, 3H, CH₃).

2-(3,4-methoxyphenyl)-5-nonyl-1,3,4-oxadiazole (3e)

IR (KBr), ν cm⁻¹: 2929 (C-H, Ar), 1610 (C=N), 1179 (C-O-C), 1249, 1030 (-OCH₃). ¹HNMR (CDCl₃) δ (ppm): 6.8-7.3 (m, 5H, Ar-H), 3.7-3.8 (s, 2H, CH₂), 2.9 (s, 2H, CH₂), 2.3 (s, 2H, CH₂), 2.1 (s, 2H, CH₂) 1.3-1.6 (s, 6H, CH₂), 1.2 (s, 2H, CH₂), 0.8 (s, 3H, CH₃).

2-(2-chloro-5-nitrophenyl)-5-nonyl-1,3,4-oxadiazole (3f)

IR (KBr), ν cm⁻¹: 2925 (C-H, Ar), 1590 (C=N), 1150 (C-O-C) 1534, 1345 (C-NO₂), 739 (C-Cl). ¹HNMR (CDCl₃) δ (ppm): 8.0-8.35 (m, 3H, Ar-H), 4.2-4.4 (s, 3H, CH₃), 3.5-3.7 (s, 3H, CH₂), 2.1-2.8 (s, 6H, CH₂), 1.2-1.8 (s, 8H, CH₂) 0.8-0.9 (s, 3H, CH₃).

2-(2,4-dichlorobenzyl)-5-nonyl-1,3,4-oxadiazole (3g)

IR (KBr), ν cm⁻¹: 2940 (C-H, Ar), 1650(C=N), 1460 (C-H, CH₂), 1385 (C-H, CH₂), 1133 (C-O-C), 721 (C-Cl str). ¹HNMR (CDCl₃) δ (ppm): 7.21-7.40 (m, 3H, Ar-H), 4.4 (s, 2H, CH₂), 3.4 (s, 2H, CH₂), 2.9-3.0 (s, 2H, CH₂), 2.12 (s, 2H, CH₂), 1.81 (s, 2H, CH₂), 1.2-1.34 (t, 8H, CH₂), 0.8-0.9 (t, 3H, CH₃).

2-(2-chlorobenzyl)-5-nonyl-1,3,4-oxadiazole (3h)

IR (KBr), ν cm⁻¹: 2930 (C-H, Ar), 1645(C-N), 1455 (C-H, CH₂), 1383 (C-H, CH₂), 1130 (C-O-C), 719 (C-Cl). ¹HNMR (CDCl₃) δ (ppm): 7.10-7.40 (m, 4H, Ar-H), 4.5 (s, 2H, CH₂), 3.3 (s, 2H, CH₂), 2.8-3.0 (s, 2H, CH₂), 2.2 (s, 2H, CH₂), 1.71 (s, 2H, CH₂), 1.2-1.4 (t, 8H, CH₂), 0.8-0.9 (t, 3H, CH₃).

Antioxidant Activity

Antioxidant activity of synthesized compounds were carried out by DPPH method using ascorbic acid as standard reference and 3 µg/ml concentration of DPPH in methanol were used. The concentrations of dilution of synthesized compounds and standard drug was made in volumetric flask by using methanol. Five concentrations i.e. 100µg/ml, 200µg/ml, 300µg/ml, 400µg/ml, 500µg/ml was considered for antioxidant activity. Methanol (1 ml) with DPPH solution (1 ml) was used as blank. 1 ml of DPPH solution was mixed with 1 ml of sample solution and standard solution separately and mixture solutions were kept in dark for 30 min and optical density was measured at 517 nm and % inhibition was calculated using the formula given below:

\[
\text{Percent inhibition of DPPH activity} = \frac{A - B}{A}
\]

Where A = Absorbance of the sample
B = Absorbance of the blank

| Table 2: Antioxidant activity of oxadiazole derivatives |
|---|---|---|---|---|---|
| Compound | 100 µg/ml | 200 µg/ml | 300 µg/ml | 400 µg/ml | 500 µg/ml |
| 3a | 87.12 | 87.73 | 88.51 | 87.80 | 88.14 |
| 3b | 32.43 | 38.51 | 34.12 | 45.95 | 31.42 |
| 3c | 35.81 | 45.94 | 39.18 | 42.56 | 41.55 |
| 3d | 84.45 | 85.13 | 85.81 | 85.47 | 84.80 |
| 3e | 85.81 | 86.79 | 86.48 | 87.06 | 86.75 |
| 3f | 78.10 | 78.23 | 78.30 | 78.43 | 78.40 |
| 3g | 50.11 | 51.13 | 50.30 | 51.20 | 52.13 |
| 3h | 37.70 | 37.62 | 39.73 | 38.90 | 38.11 |
| Ascorbic acid | 86.82 | 87.53 | 88.17 | 88.10 | 89.52 |

RESULTS AND DISCUSSION

The reaction progress and purity of compounds were confirmed by TLC. The structures of the synthesized compounds (Scheme 1) were characterized.

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physiologically (Table 1) and by IR and $^1$H NMR and found in good agreement with the spectral data.

The antioxidant activity of the synthesized compounds and the standard was assessed on the basis of the radical scavenging effect of the stable 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical activity. DPPH assay was carried out for compounds 3a-h at different concentrations from 100 to 500 µl/ml concentration. The compounds 3a, 3d and 3e showed excellent antioxidant activity in comparison to ascorbic acid whereas 3b, 3c and 3h showed least free radical inhibition (Table 2).

**CONCLUSION**

The antioxidant activity of synthesized compounds revealed that oxadiazoles containing 4-fluorophenyl and 3,4-dimethoxyphenyl group at C-5 position of 1,3,4-oxadiazole ring have better result as compared to the standard drug and can be selected for further studies.

**REFERENCES**


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