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Green synthesis of pharmaceutically important 1, 3, 4-thiadiazole derivative of Guar gum as an antimicrobial agent

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Abstract
Green colour signals to proceed and green chemistry signals to sustain. In present study a novel thiadiazole derivative of Guar gum is synthesized by a sustainable greener method i.e. microwave assisted synthesis. Thiadiazole constitutes a class of heterocyclic compounds with good pharmacological profile. Guar gum is used as an emulsifier, thickener and stabilizer in various food and cosmetic industries. The newly synthesized derivative was characterized by IR, H^1 NMR and mass spectrometry analysis. Antimicrobial activity was also studied.

Keywords: Guar gum, 1, 3, 4. thiadiazole, microwave assisted synthesis, antimicrobial activity

1. Introduction
Guar gum is a potential aspirant of naturally occurring biodegradable polymer due to its non-toxicity, biodegradability, biocompatibility, stability over wide pH range and modifying rheological properties [1, 4]. Guar gum (*Cymopsis tetragonoloba*) represents Galactomannan family of polysaccharides. Chemical modification of Guar gum diversifies and enhances its applications and functionality. In present study this polysaccharides is derivatized by thiadiazole nucleus using microwave irradiation.

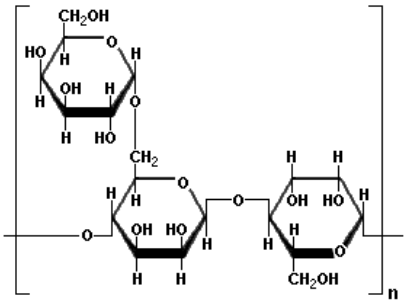

Fig 1: Guar gum structure

Thiadiazole compounds are metabolised by routine biochemical reactions and are non-carcinogenic in nature [5, 8]. they are known to have unique antibacterial and antioxidant properties [9, 10]. These reports prompt us to synthesize novel derivative of thiadiazole which would be effective against various strains of microorganisms [11, 14].

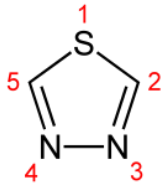

Fig 2: 1, 3, 4-thiadiazole

The significant outcome of Microwave assisted chemistry endeavours which have resulted in development of synthetic protocols for drugs and fine chemicals. The use of emerging Microwave assisted chemistry in conjunction with greener reaction media dramatically reduces chemical wastes and reaction time. This protocol offers several advantages including its greenness with respect to mild conditions, good yield of products and operational simplicity [15, 16].

2. Materials
Guar (200 mesh size) was procured from local industry. All AR grade chemicals used were procured from Sigma Aldrich, Loba Chemicals, and Ases chemical works. The bacterial and fungal strains used for evaluation of antimicrobial activities, were obtained from S.N. Medical College, Jodhpur.

3. Methods
3.1 Synthesis of epoxy ether of Guar
1 mole of guaran powder was slurred in DMSO solvent in a round bottom flask. Then 50% aqueous NaOH was added in the slurry to make the reaction mixture alkaline, and the mixture was constantly magnetically stirred at 45°C for 2 hours. Further 1 mole of epichlorohydrin was added gradually with continuous stirring and the pH was adjusted to 9-10 then this reaction mixture was subjected to microwave for 15 minutes. Later, the compound was filtered on vacuum pump with 80% aqueous methanol containing few drops of nitric acid to remove inorganic impurities of chloride ion and excess of alkali. (Fig-2)

3.2 Synthesis of 5-(aryl amino)- 2-sulfanyl 1, 3, 4-thiadiazole
0.1 mole of aniline was dissolved in 20 ml of ammonia solution to which 0.1 mole of carbon disulphide was gradually added with constant stirring. The temperature of the solution was kept below 30°C. 20-25 ml of ethanol was then

added and the stirring was continued till all the carbon disulphide dissolved. The reaction mixture was then allowed to stand for 2 hours.

Equimolar quantity of sodium hydroxide and monochloroacetic acid were taken, dissolved separately in water and cooled. After cooling, mix the solutions to obtain sodium salt. This sodium chloro acetate solution was added to the reaction mixture followed by the addition of 10 ml of 50% hydrazine hydrate. The mixture became warm that was cooled. After cooling it was filtered, dried and recrystallized with ethanol [17]. (Fig-3)

3.3 Synthesis of thiadiazole derivative of Guar Gum

Now equimolar quantities of above synthesized thiadiazole and 1, 2- epoxy propyl guar is mixed and the mixture was subjected to microwave irradiation for 10-12 minutes. The so formed derivative was filtered and purified with ethanol. (fig 4).

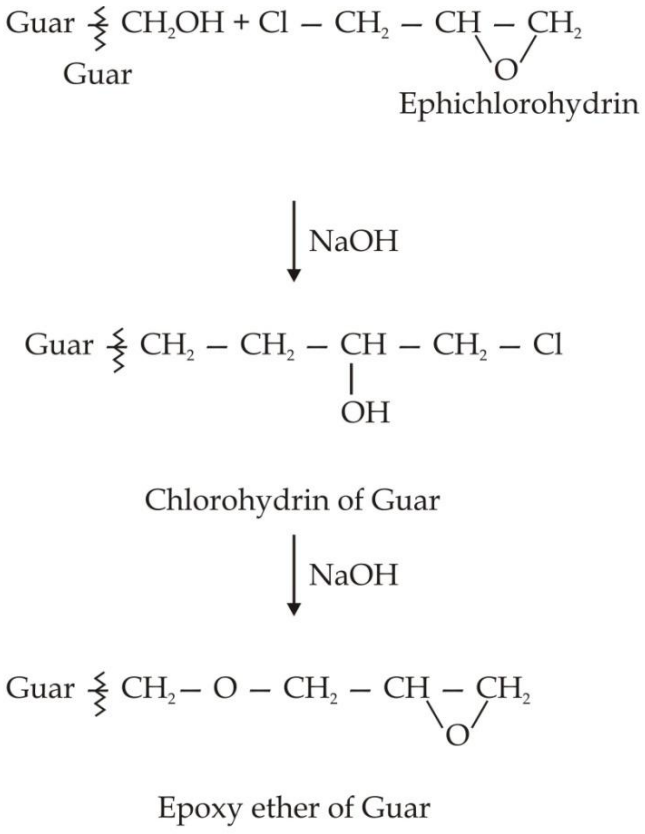

Fig 3: Synthesis of epoxy ether of Guar

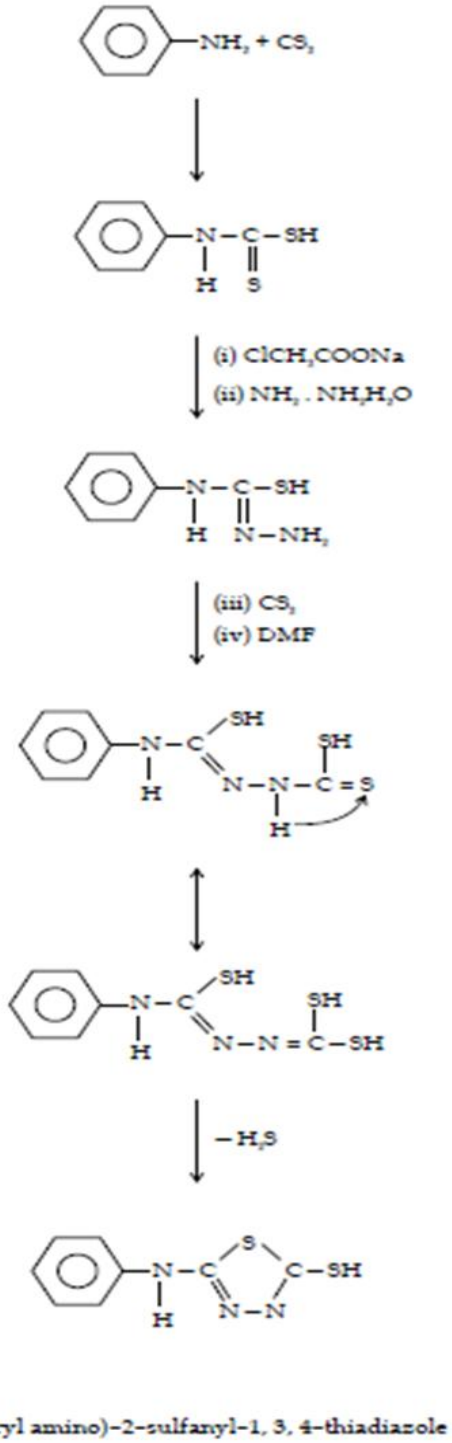

Fig 4: Synthesis of 5-(aryl amino)- 2-sulfanyl 1,3,4- thiadiazol

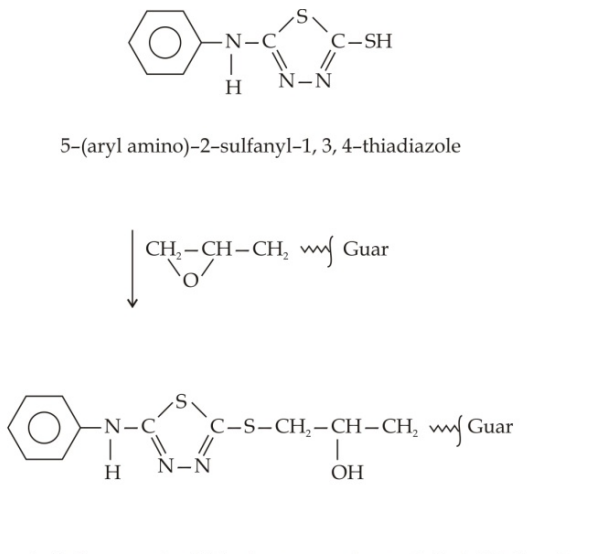

Fig 5: Synthesis of thiadiazole derivative of Guar gum

4. Characterization

Melting point of the compound is determined in open capillary tube and is uncorrected. The newly formed derivative was characterized by FTIR spectroscopy, H1 NMR Spectroscopy and Mass spectrometry.

5. Antimicrobial Activity

An anti-microbial is a substance that kills or inhibits the growth of microorganisms such as bacteria, fungi, or protozoan. Thiadiazole is an important heterocyclic nucleus and it has occupied a pivotal position in medicinal chemistry because it is having a broad spectrum of pharmacological activities especially potent antimicrobial activity against a wide variety of microbes like bacteria and fungi [18].

The antibacterial and antifungal activities of newly synthesized compounds were evaluated using well diffusion assay. A 24 and 48 hours old culture of selected bacteria and fungi respectively were mixed with sterile physiological saline (0.9%) and the turbidity was adjusted to the standard inoculums of Mc Farland scale (0.5 for bacteria and 2.0 for fungi). Petri plates containing Muller-Hinton Agar was used for antibacterial and Muller Hinton Agar (containing methylene blue and glucose) was used for antifungal activity. The inoculums were spread on the surface of the solidified media. Wells of approx 6 mm were dig on the sterile agar plate and solution of the derivative is filled in a well. DMSO solution, as control is filled in another well. Ampicillin and Voriconazole were used as standard drugs for bacteria and fungi respectively. Plates inoculated with bacteria were incubated for 24 hours at 37°C and with fungal culture was incubated for 36-48 hours at 25°C. The inhibition zones were measured by transparent ruler [19].

6. Results & Discussion

Successful microwave assisted synthesis of Guar thiadiazole derivative was done without using any catalyst. The yield of the product is greater (70%) than the yield obtained (55%) by conventional heating method.

6.1 FT-IR Analysis

IR Spectra was recorded with BRUKER spectrophotometer. The spectrum of the newly synthesized compound shows a peak at 1012.80 for C-O stretching. Peaks at 1241.90 and 1515.08 represent C-N stretching and aromatic- N-H bending respectively. A distinctive peak at 2675.04 denotes the presence of -C-S stretching. One peak at 3375.54 shows -NH stretching in secondary amines. Another peak at 3520.95 is due to -OH stretching (fig 6)

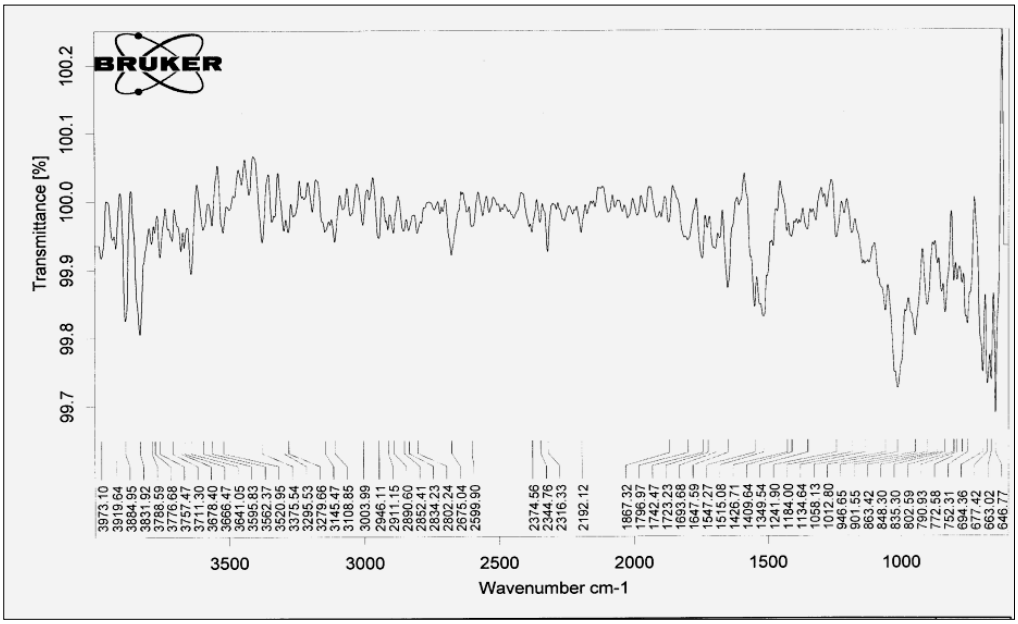

Fig 6: IR Spectra

6.2 H^1 NMR Analysis: NMR

Spectra was determined by Bruker AV-II 300 MHz FT-NMR Spectrometer. The compound was dissolved in DMSO. The interpretation shows peak at δ3.46 for aromatic amine proton (C_6H_5N-H). Other peaks at δ2.5 to 3.5 may be due to methylene protons and upfield signal at δ 7.35 is due to aromatic proton (Ar-H). (fig 7)

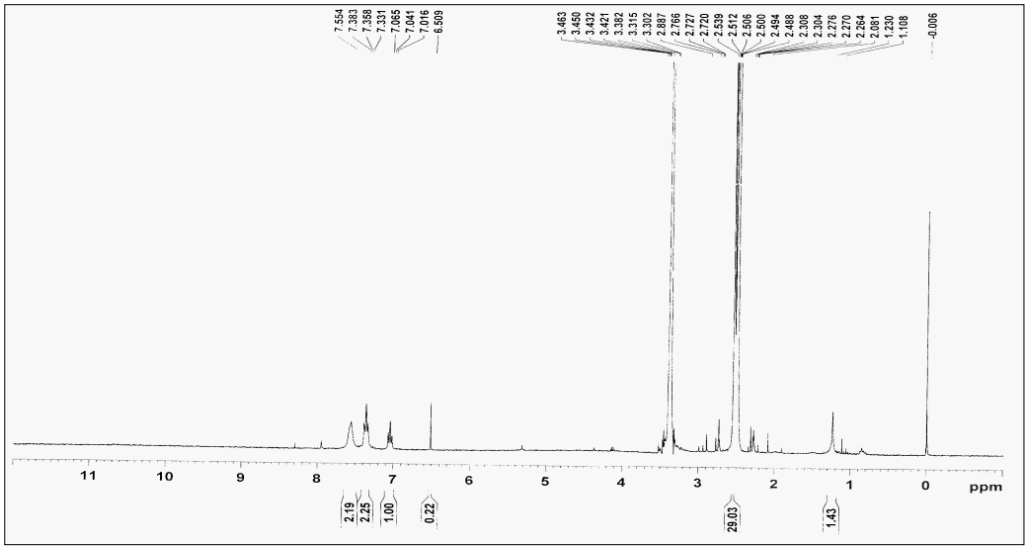

Fig 7: H^1 NMR Analysis

6.3 Mass spectral Analysis

DART-MS was recorded on a JEOL-AccuTOF JMS-T1OOLC Mass spectrometer having a DART (*Direct analysis in real time*) source. The compound was subjected as such in front of DART source. Dry Helium was used with 4 LPM flow rate for ionization at 350°C. The orifice 1 was set at 28 V. Mass spectral analysis- Base peak at 157.07 (fig-8)

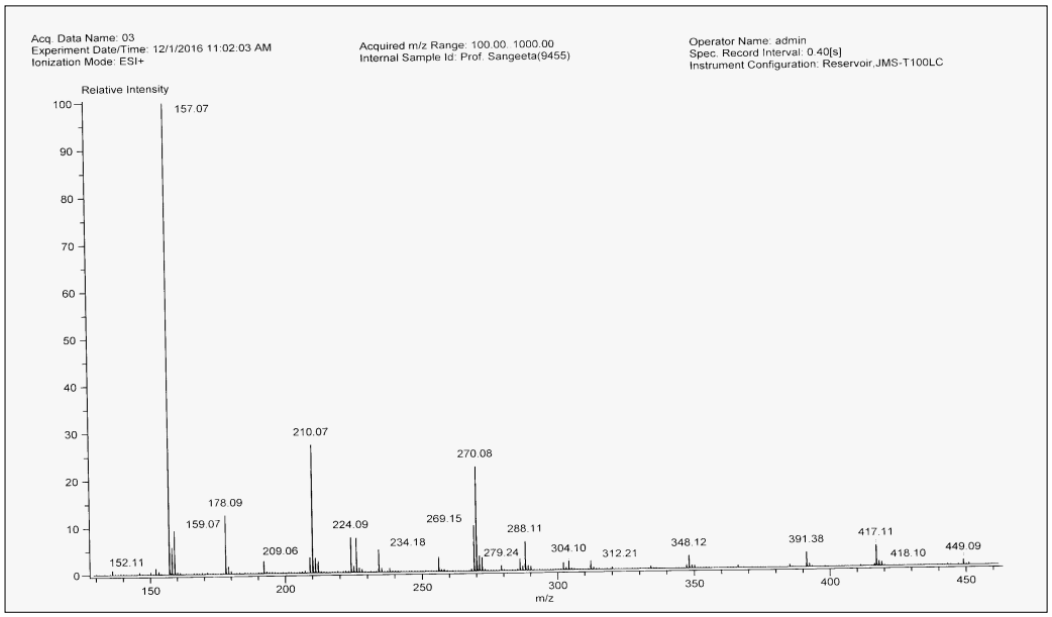

Fig 8: Mass spectra

6.4 Antimicrobial Activity

The antimicrobial evaluation of the newly synthesized Guar derivative states that the compound exhibits significant activity against gram negative bacteria and gram positive bacteria (Table 1). It shows inhibition zone against *Escherichia coli, klebsiella pneumonia, Staphylococcus aureus* and no zone of inhibition against *Pseudomonas aeruginosa.* Fungal strains like C*andida albicans, Candida parapsilosis* do not grow in presence of the compound.

Table 1: Antibacterial activity of 1, 3, 4 thiadiazole derivative of Guar gum

S. No.	Bacterial strains	Type	Zone of Inhibition
1.	*Escherichia coli*	Gram Negative	6mm
2.	*klebsiella pneumonia*	Gram Negative	13mm
3.	*Staphylococcus aureus*	Gram Positive	2mm
4.	*Coagulase negative staphylococci(CONS)*	Gram Positive	5mm

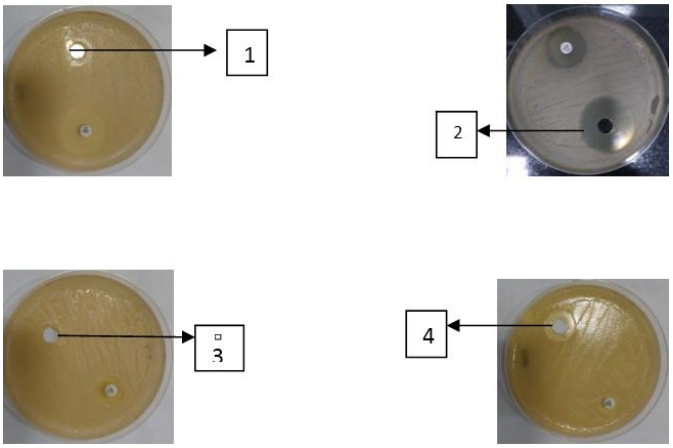

Fig 9: Photographs [A], [B], [C] & [D] showing antibacterial activity

Table 2: Antifungal activity of 1, 3, 4 thiadiazole derivative of guar gum

S. No.	Fungal Strains	Zone Of Inhibition
1.	Candida albicans	13mm
2.	Candida parapsilosis	15mm

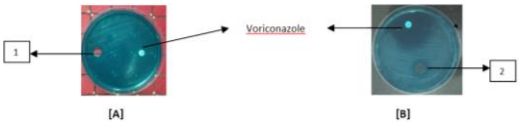

Fig 10: Photographs [E] & [F] showing antifungal activity

Conclusion

Microwave technology has become easy for medicinal chemistry to apply in a beneficial and reproducible manner providing technique that is widely embraced. The synthesized compound showed significant antimicrobial activity. So there is huge scope to extend the applicability of this technique.

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References

1. Properties of Guar gum:http://www.guargum.biz/guargum_properties.html
2. Iqbal DN, Hussain EA. Green biopolymer Guar gum and its derivatives, IJPBS, 2013; 4(3):423-435.
3. Iqbal DN, Hussain EA, Naz N. Synthesis and characterization of Guar gum derivatives with antioxidant moieties, Int J Pharm Bio Sci, 2013; 4(4):305-316.
4. Gupta A, Verma DK. Guar gum and their derivatives:a research profile, IJAR, 2014; (1):680-690.
5. Chawla. *et al.* Review on Chemistry and Biological activities of thiadiazole derivatives, AJPTR, 2014; 4(1):213-233.
6. Kaur H. *et al.* Synthesis and antimicrobial evaluation of thiadizole derivatives, Der Pharma Chemica, 2014; 6(2):66-69.
7. Desai NC, Bhavsar AM, Shah MD, Saxena AK. Synthesis and QSAR studies of thiosemicarbazides, 1,2,4-triazoles, 1,3,4-thiadiazoles and 1, 3, 4-oxadiazoles derivatives as potential antibacterial agents. Ind J Chem, 2008; 47:579-589.
8. Polshettiwar V, Varma RS. Greener and rapid access to bio-active heterocycles, one pot solvent free synthesis of 1, 3, 4-oxadiazoe and 1, 3, 4-thiadiazole. Tetrahedron Letters, 2008; 49:879-883.
9. Thomasco LM, Gadwood RC, Weaver EA, Ochoada JM, Ford CW, Zurenko GE. *et al.* The synthesis and antibacterial activity of 1, 3, 4-thiadiazole phenyl oxazolidinone analogues, Bioorg. Med. Chem. Lett, 2013; 13(23):4193-4196.
10. Bak B, Cristensen D, Nygard LH, Lipschitz L, Andersen JR. Microwave spectra of 1,3,4- thiadiazole and [34S]1,3,4-thiadiazole. Dipole moment of 1, 3, 4-thiadiazole, Journal of Molecular Spectroscopy, 1962; 9:225-227.
11. Kharb R, Kaur R, Sharma AK. Therapeutic impact of novel thiadiazole scaffolds in drug design as potent antimicrobial agents, IJRPC, 2014; 4(4):1028-1038.
12. Ahmed T, Singh AK, Jaiswal N, Sharma D. Synthesis of pharmacological activity of thiadiazole derivative: a review. International research journal of pharmacy. 2012; 3(3):70-82.
13. Matysiak J, Malinski Z. 2-(2, 4-Dihydroxyphenyl)-1, 3, 4-thiadiazole analogues: antifungal activity in vitro against Candida species, Bioorg. Khim. 2007; 33(6):640-647.
14. Asif M. Biological potential of thiadiazole substituted compounds, American journal of current organic chemistry, 2014; 1:17-36.
15. Sah P, Gharu CP. Synthesis, characterization and antimicrobial evaluation of Schiff bases of 4-thiazolidinone bearing thiadiazole moiety, J. Cur. Pharm. Res. 2012; 9(1):44-48.
16. Kumar R, Setia A, Mahadevan N. Grafting modification of the polysaccharides by the use of microwave radiation, International journal of recent advances in pharma research, 2012; 2(2):45-53.
17. Giri S, Singh H. J Indian Chem. 1967; 44:145-147.
18. Farshori NN, Banday MR, Ahmad A, Khan AU, Rauf A. Synthesis, characterization, and in vitro antimicrobial activities of 5-alkenyl/hydroxyalkenyl-2-phenylamine-1,3,4-oxadiazoles and thiadiazoles. Bioorg Med Chem Lett. 2010; 20:1933-1938.
19. CLSI, Method for Antifungal Disk Diffusion Susceptibility Testing of Non- dermatophyte Filamentous Fungi, Approved guideline, CLSI document M51- A. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 2010.