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SYNTHESIS OF BIOLOGICALLY ACTIVE 3-ALKYL OR 3-ARYL CHROMON SUBSTITUTED TRIAZOLO THIADIAZOLES

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Abstract:-"Chromone" is regarded as a significant unit of chemical because a large number of its variants with side chain at various locations form a diverse range of heterocyclic naturally occurring oxygen compounds called as flavonoid. Two thiadiazole derivatives were synthesized using different reagents and procedures and then were evaluated to check their antibacterial; and antifungal activity. Both the compounds were synthesized and characterized using IR. The compounds were found to possess antibacterial and antifungal activity to a good extent. They were effective against two out of three bacterial strains that we used to test. Thiadiazole derivative can be effective and potent candidates for antimicrobial activity and can be further used to treat microbial infections.

Keywords: Alkyl and aryl, Chromone, Flavones, Heterocyclic compounds, Thiadiazols **,** flavonoids .

Introduction

"Chromone" is regarded as a significant unit of chemical because a large number of its variants with side chain at various locations form a diverse range of heterocyclic naturally occurring oxygen compounds called as flavonoid. Other subgroups of this family of chemicals include 3-phenylchromones or others (flavones). 2-phenylchromones are a kind of isoflavones (flavanol), dihydro derivatives of flavanones, 3-phenylchromone (isoflavones) 3-hydroxyflavones, flavanones, or isoflavones [1, 2].

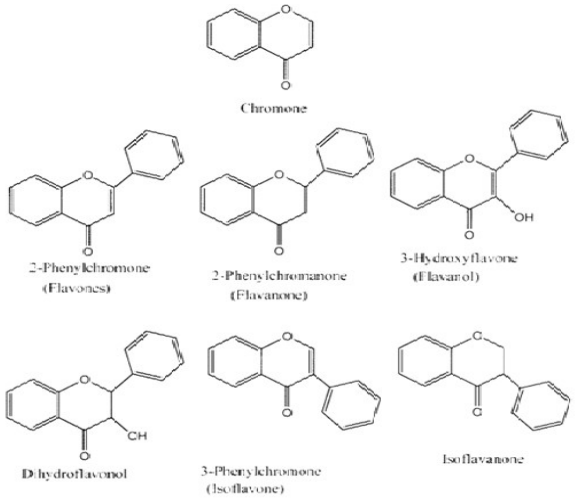

Figure -1 Showing structure of "flavones and isoflavones"

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The chromone-3-formylchromone) chromone-3-carboxaldehyde was a fascinating unit although it might conduct condense with the number of compounds using its function of aldehyde function, or it can be engaged in a Michael type reaction with a molecule carrying an active methylene group.

These compounds have received a lot of attention in recent years since they have been discovered to have a variety of significant pharmacological characteristics, such as anti-HIV activity or anticancer. In addition, the literature lists a significant number of synthesized compounds containing the chromone unit that exhibit a variety of intriguing pharmacological properties. Here's a quick rundown as follows.

Klutchko et al. discovered that 3-formylchromone or 6-bromo-3-formylehromone had antiallergic action in rates [3].

Re et al. [4] reported 3-hydroxymethyl-8-methoxychromone inhibits redeem-mediated responses in the bronchopulmonary system or skin with a high specificity.

According to Kapoor et al. [5] found "3-(arylaminomethylene)-2.3-dihydro-2-substituted 4H-1-benzopyron-4-ones" show diuretic action. 6-substituted [1]benzopyrano(2.3-b)[1.5]benzodiazepine-13-ones exhibit significant moderate anti-inflammatory action or analgesic, according to Devi et al. [6]. The substances [1,5] "benzodiazepine-l3-ones, 11 -dihydro-7-nitro[l]benzopyrano [2,3-b]" 6-aIkyl/araIkyl-5a. and 11 "-dihydro-7-nitro[l]benzopyrano[2,3-b] N-aIkyl/aralkyl-3-nilro-o-phenylenediamine" was discovered to have anti-inflammatory properties, analgesic, or hypotonic.

Methodology:-

1.1 Synthesis and characterization of "3-Alkyl-6-(chromon-3-yl)-5,6-dihydro-s-triazolo[3,4-b][1,3,4]thiadiazoles"

- **Synthesis procedure**

Chromone-3-carboxaldehyde has been used to make a range of chromone-containing heterocyclic compounds including sulfur and nitrogen. As a result, [l.3.4]thiadiazoles connected to the unit of chromone were taken up. "6-(Chromon-3-yl)"–5.6-dihydro-s-triazolo[3.4-b][1.3.4]thiadiazole", the first example was chosen. Under anhydrous circumstances, the chromone-3-carboxaIdehyde needed for the reaction were made by reacting "2-hydroxyacetophenone" to "dimethylformamide" in the influence of "phosphorus oxychloride". This was synthesized by "4- amino-5-mercapto-l.2.4-triazole" in medium of dry benzene below the reflux of utilizing the dean equipment of stark in the influence of p-toluenesulphonic acid. TLC was used to check the progress of the reaction, which had been found to be finished in 9.0 hours. After concentration and cooling, the reaction mixture yielded a solid light yellow-colored, which would recrystallize to extract ethanol to produce a light-colored crystal (71 percent yield).

- **Characterization by TLC**

TLC was used to monitor the reaction's development, and it was discovered that the reaction took 1.5 minutes to finish (6x15 sec). The reaction mixture has to be cooled down. After

dissolving a sample solution with cold water, the solid that separate were re-crystallized from ethanol to produce "6-(chromon-3-yl)-5.6-dihydro-s-triazolo [3.4-b] [1,3.4] tthiadiazole".

1.2 Synthesis and characterization of "3-Aryl-6-(chromon-3-yl)- 5,6-dihydro-s-triazoIo[3,4-b] [l,3,4]thiadiazoles"

- **Synthesis procedure**
  "6-(chromon-3-yl)-3-(3-methylphenyl)- 5.6-dihydro-s-triazolo thiadiazole" has remained used to make the suggested chemical. The dean bright equipment has been used to interact chromone-3-carboxaldehyde or "4-amino-3-(3-methylphenyl)-5-mereapto-l.2.4-triazole" throughout influence of during reflux in the dry benzene of medium. TLC has been used to monitor the reaction's progression, so it was discovered that the reaction took 8.0 hours to complete. After doing up the response, a light yellow-coloured solids were obtained, which has been ethanol recrystallized to produce crystals light yellow-coloured crystals (produce 72%, m.p. 214-215ºC).
- **Characterization by IR**
  IR spectroscopy was used for the characterization of both the compounds synthesized.

1.2 Antibacterial Activity

Compounds' antibacterial activity against S. aureus, *Pseudomonas aeruginosa*, or E. coli, were evaluated in vitro using the paper disc technique. Dispersing the chemical in DMF yielded solutions of various concentrations. The 6 mm bacterial suspension dishes were steeped in such liquids but then inserted into bacteria-inoculated nutrient agar slants. These cells were placed at 37°C for 24 hours before being tested for bacterial growth suppression. The zone of inhibition was observed in mm are shown on the plates. The antibacterial activity of ciprofloxacin was studied as a standard.

1.3 Antifungal Activity

The paper-disc technique has been used to test antifungals in vitro versus (C. albicans at an intensity of 1000 ppm, 500 ppm & 100 ppm, respectively, as described throughout the antifungal purpose. The antifungal activity of study of fluconazole being as a standard. There was no self-consciousness zone in the DMF on its own [9].

2. Results

2.1 Formation of "3-Alkyl-6-(chromon-3-yl)-5,6-dihydro-s-triazolo[3,4-b][1,3,4]thiadiazoles"

The above procedure yielded the 3-Alkyl-6-(chromon-3-yl)"- "5,6-dihydro-s-triazolo" "[3,4-b][1,3,4]thiadiazole.

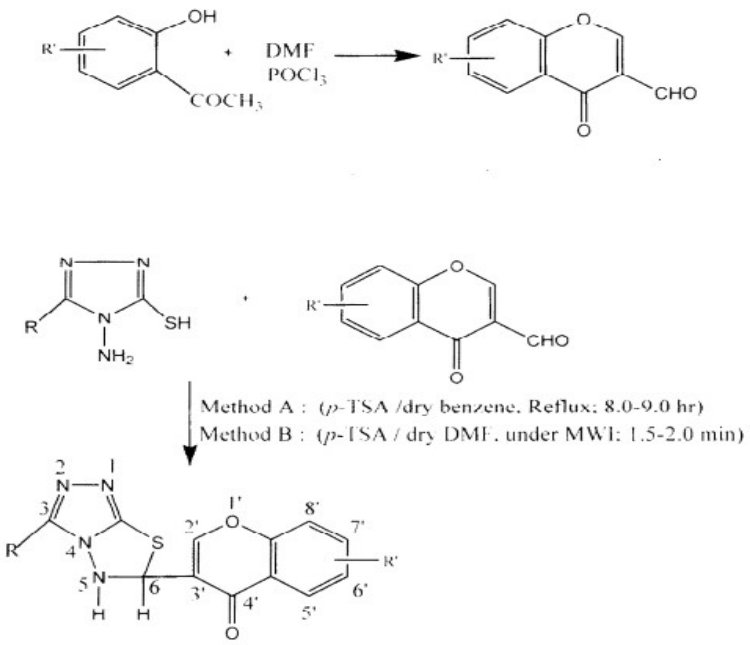

Fig 2 - "3-Alkyl-6-(chromon-3-yl)- 5,6-dihydro-s-triazolo[3,4-b][1,3,4]thiadiazoles"

2.2 IR results of "3-Alkyl-6-(chromon-3-yl)- 5,6-dihydro-s-triazolo[3,4-b][1,3,4]thiadiazoles"

The compound's IR had shown fascination at 31 11 cm-1 due to "N-II stretching", fascination at 3050 cm-1 due to "C-H stretching", assimilation at 1640 cm'1 due to >0-0 group in the substance, absorption at 1620 cm'1 due to C=N stretching, absorption at 1546 cm'1 owing to stretching of C=C, assimilation at 1461. 1199 cm-1 owing to stretching of assimilation at 1546 cm-1 or C-N, Elimination of absorbance in the range 2700-2900 cm-1 (normally two bands owing to fermi resonance) showed the presence of -Cl 10 in the process thus confirmed the structure of cyclic. The elemental study of this structure backed it up even more.

2.3 Formation of "3-Aryl-6-(chromon-3-yl)- 5,6-dihydro-s-triazoIo[3,4-b] [l,3,4]thiadiazoles"

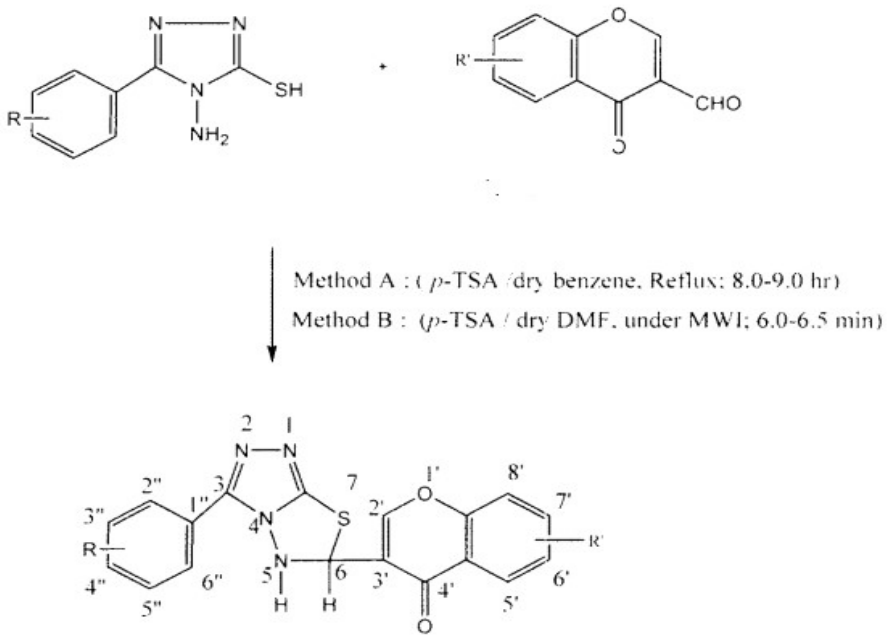

Fig 3 - "6-(chromon-3-yl)-3-(3-methylphenyl)- 5.6-dihydro-s-triazolo thiadiazole"

2.4 IR results of "3-Aryl-6-(chromon-3-yl)- 5,6-dihydro-s-triazoIo[3,4-b] [l,3,4]thiadiazoles"

A structure's Infrared had shown intake at owing to "N-H stretching", assimilation at "3065 cm'1" owing to fragrant "C-H stretching", assimilation at 2930 cm'1 owing to aliphatic C-H stretching, assimilation at 1651 cm'1 confirmed the presence of the >(7=0 group in the chemical agent, permeability at 1619 cm'1 suggested the existence of C-N stretching, and absorption at 1560 cm'1 indicated the presence of C=C Absence of absorption in the range 2700-2900 cm'1 (normally two bands owing to fermi resonance) showed the participation of-CUO in the process & confirmed a cyclic structure [10].

2.5 Antibacterial activity

There was no zone of inhibition in the DMF itself. Table 1 shows the zones of inhibition exhibited by different drugs [11, 12].

Table 1 – Antibacterial activity data of 3-alkyl and 3-aryl-6-(chromon-3-yl)-5,6-dihydro-s-triazolo[3,4-b][1,3,4]thiadiazole at different concentration (Diameter of Zone of Inhibition in mm)

	E.coli			S. aureus			P. aeruginosa		
Compound	1000 Ppm	500 Ppm	100 ppm	1000 ppm	500 ppm	100 ppm	1000 ppm	500 ppm	100 Ppm
1	13	12	14	15	13	12	-	-	-
2	2	12	14	13	13	-	-	-	-
Std (Cip)	21	20	18	28	19	18	28	28	20

6 mm diameter disc Ciprofloxacin is the gold standard (cip). The following conclusions were made from table-l.

i. "6-(6-methylchromon-3-yl) substituted 3-alkyl-5,6-dihydro-s-triazolo[3,4-b][l,3,4] thiadiazoles" was observed to be more active against S. aureus.
ii. "6-(6-methylchromon-3-yl)" substituted "3-aryl-5,6-dihydro-s-triazolo[3,4-b][1,3,4]thiadiazoles" was observed to be more activate towards E. coli at 100 ppm concentration.
iii. Both the compounds were inactive against P. aeruginosa.

2.6 Antifungal activity

Table 1 – Antifungal activity data of 3-alkyl and 3-aryl-6-(chromon-3-yl)-5,6-dihydro-s-triazolo[3,4-b][1,3,4]thiadiazole at different concentration (Diameter of Zone of Inhibition in mm

Compound	1000 ppm	500 ppm	100 ppm
1	15	14	11
2	16	14	11
Std (Flu)	19	18	12

6 mm diameter disc Fluconazole is the gold standard (flu). The resulting conclusions was made from table-l.

i. "6-(chromon-3-yl) substituted 3-aryl-5,6-dihydro-s-triazolo[3,4-b][1,3,4] thiadiazoles" was observed to indicate potent antifungal activity.

ii. "6-(chromon-3-yl)", 6-(6-methylchromon-3-yl) or 6-(7-methoxychromon-3-yl) exchanged "3-alkyl-5.6-dihydro-s-triazolo [1,3,4] thiadiazoles" was observed to possess antifungal activity at 1000 ppm concentration.
iii. Both the compounds were less active at 100 ppm concentration.

3. Discussion

During recent years there has been intense investigation of different classes of thiadiazole compounds, many of which known to possess interesting biological properties such as antimicrobial, antihypertensive, local anesthetic, anticancer, and hypoglycemic activities. These important biological activities encouraged several research groups to find out different methods for synthesis of new thiadiazoles using different synthones, such as chromones, thiosemicarbazides, thioacylhydrazines, and bithioureas.

In this study, we synthesized 2 derivatives of 1,3,4 thiadiazoles. Alkyl and aryl group was substituted at the 3rd position of thiadiazols along with chromone substituent at 6th position. The compounds were then characterized using IR and their antimicrobial property was evaluated.

In similar to our study, Mithun et al. 2007 [13] also synthesized derivatives of thiadiazoles and tested them for their antimicrobial properties. 7-(substituted aryl/aryloxy methyl-3-(4-methylthiobenzyl)-4*H*-1,3,4-thiadiazolo [2,3-*c*]-1,2,4-triazin-4-ones by reacting 4-amino-6-(4-methylthiobenzyl)-3-mercapto-1,2,4-triazin-5(4*H*)-one with substituted benzoic acids/aryloxy acetic acids in the presence of phosphorus oxychloride. The antibacterial and antifungal activities were carried out and all the tested compounds were possessing moderate activity for both microbes.

Similarly, Abdelhamid et al. (2015) [14] have prepared 1,3,4-thiadiazolines containing a chromone moiety and 5-{1-[4-substituted-5-phenyldiazenyl)(1,3-thiazol-2-yl]-5-phenyl-2-pyrazoline-3-yl)}-4-methoxybenzo[*b*]-furan-6-ol. These compounds showed some extent of antimicrobial properties.

We found that "3-alkyl--6-(chromon-3-yl)-5,6-dihydro-s-triazolo[3,4-b][l,3,4]thiadiazoles" was more active against S. aureus. Both the compounds were found to be inactive against P. aeruginosa. They both showed antifungal activity at 1000 ppm concentration.

Conclusion

Need for synthesizing new compounds to cope up with the microbial resistance is a primary and major concern in drug industry. Different thiazole derivatives have shown to possess microbial activity at different extent and hence they are a suitable candidate for creating antimicrobial compounds. In this research, we prepared two derivatives of 1,3,4 thiadiazoles and characterized them using IR and tested them for antimicrobial property. Both of the compounds were found to have a effective level of antibacterial and antifungal activity and hence can be further studied to determine their full potential.

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