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Statistical Comparison of Antimicrobial Activity of 1, 5-Benzothiazepines Derivatives

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ABSTRACT:

Comparative statistical studies were carried out on number of compounds of 8-substituted-2,5-dihydro-2-(3,4-dimethoxyphenyl)-4-(phenyl/4-chlorophenyl/2-thienyl/4-methylphenyl)-1,5-benzothiazepines by ANOVA techniques using SPSS to find out the difference between the effects of substituents on yield of compounds and on antimicrobial activities i.e. antibacterial & antifungal activity. No significant difference between the effects is formed for substituent on yield and zone of inhibition but remarkable difference between the effects was found on activity index.

Keywords: Methoxyl substituent, 1,5-Benzothiazepines, Antimicrobial Activity, ANOVA, SPSS

[I] NTRODUCTION

The 1,5-benzothiazepines are important heterocyclic compounds in drug research since they possess diverse bioactivities [1-6,16,17] like antiulcer, analgesic, vasodepressant, antihypertensive, antiamnesia and antidemnetia, antibacterial & antifungal activity etc. The first molecule of 1,5-benzothiazepine, used clinically worldwide was diltiazem, followed by clentiazem and Siratiazem for their cardiovascular action. All these molecules were found to possess methoxyl group as a substituent in 1,5-benzothiazepine nucleus. Some of bicyclic and tetracyclic 1,5-benzothiazepines having methoxyl groups in the nucleus in different proportions were synthesized and reported [7-10,15] presuming that methoxyl group acts as pharmacophore. Therefore, it was thought that the 2,4,8-substituted-2,5-dihydro-1,5-dihydrobenzothiazepines having methoxyl groups as substituent are useful compounds [11-14] in the lead discovery, statistical studies were carried on number of compounds having methoxyl substituents to compare the effect of substituents on yield and antibacterial and antifungal activities using ANOVA techniques by SPSS.

[II] MATERIAL & METHODS

As we assumed that methoxyl group act as pharmacophore or enhance pharmacological activity of 1,5-benzothiazepine compounds [8-

14], four series of 1,5-benzothiazepines with common substituent as 3,4-dimethoxyphenyl were chosen to carried out study of stastical comparisons. Four series of 1,5-benzothiazepines are "8-substituted-2,5-dihydro-2-(3,4-dimethoxy-phenyl)-4-phenyl-1,5-benzothiazepines [11]", "8-substituted-2,5-dihydro-2-(3,4-dimethoxyphenyl) -4-(4-chlorophenyl)-1,5-benzothiazepines [12]", "8-substituted-2,5-dihydro-2-(3,4-dimethoxy-phenyl)-4-(2-thienyl)-1,5-benzothiazepines [13]" and "8-substituted-2,5-dihydro-2-(3,4-dimethoxy-phenyl)-4-(4-methylphenyl)-1,5-benzothiazepines [14]". These compounds were compare for their yield by same experimental methods and antimicrobial activity i.e. antibacterial and antifungal activity with same gram negative (*Pseudomonas aeruginosa*) and gram positive bacteria (*Staphylococcus aureus*) and same fungus (*Candida albicans*).

All these compounds were synthesized [11-14] by reacting equimolar quantities of 5-substituted-2-aminobenzenethiols with chalcone or α,β-unsaturated heterocyclic ketone in dry ethanol saturated with dry HCl gas in one step in 55-70% yield (**Table 1**).

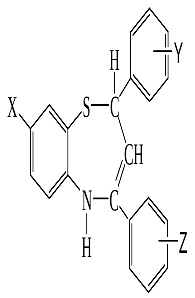

Fig: 1. 2, 4, 8-Substituted 1,5-benzothiazepines

Table 1. Yields of 1,5-Benzothiazpine Derivatives

Compd	Series	**Substituents**			**Yield (%)**
		X	**Y**	**Z**	
FS1	1	F	3,4-$(OCH_3)_2$	4-Phenyl	55
FS2	1	Cl	3,4-$(OCH_3)_2$	4-Phenyl	57
FS3	1	Br	3,4-$(OCH_3)_2$	4-Phenyl	60
FS4	1	CH_3	3,4-$(OCH_3)_2$	4-Phenyl	62
FS5	1	OCH_3	3,4-$(OCH_3)_2$	4-Phenyl	65
FS6	1	OC_2H_5	3,4-$(OCH_3)_2$	4-Phenyl	61
SS1	2	F	3,4-$(OCH_3)_2$	4-ChloroPhenyl	61
SS2	2	Cl	3,4-$(OCH_3)_2$	4-ChloroPhenyl	63
SS3	2	Br	3,4-$(OCH_3)_2$	4-ChloroPhenyl	55
SS4	2	CH_3	3,4-$(OCH_3)_2$	4-ChloroPhenyl	61
SS5	2	OCH_3	3,4-$(OCH_3)_2$	4-ChloroPhenyl	68
SS6	2	OC_2H_5	3,4-$(OCH_3)_2$	4-ChloroPhenyl	56
TS1	3	F	3,4-$(OCH_3)_2$	2-Thienyl	55
TS2	3	Cl	3,4-$(OCH_3)_2$	2-Thienyl	57
TS3	3	Br	3,4-$(OCH_3)_2$	2-Thienyl	60
TS4	3	CH_3	3,4-$(OCH_3)_2$	2-Thienyl	62
TS5	3	OCH_3	3,4-$(OCH_3)_2$	2-Thienyl	65
TS6	3	OC_2H_5	3,4-$(OCH_3)_2$	2-Thienyl	61
FO1	4	F	3,4-$(OCH_3)_2$	4-Methylphenyl	60
FO2	4	Cl	3,4-$(OCH_3)_2$	4-Methylphenyl	67
FO3	4	Br	3,4-$(OCH_3)_2$	4-Methylphenyl	62
FO4	4	CH_3	3,4-$(OCH_3)_2$	4-Methylphenyl	70
FO5	4	OCH_3	3,4-$(OCH_3)_2$	4-Methylphenyl	62
FO6	4	OC_2H_5	3,4-$(OCH_3)_2$	4-Methylphenyl	64

All these compounds were reported [11-14] to possess relative antibacterial and antifungal activity. The activity was tested against bacteria, S. *aureus*, *P. aeruginosa* and fungus, *C. albicans* by using reference compounds gatifloxin, natilmicin and fluconazole respectively. The paper disc method was used at the concentration of 100µg/disc. The zone of inhibitions for the test and reference compounds were measured in millimeters in 40 hr incubation period and compared to get the results in the form of activity index.

$$\text{Activity Index} = \frac{\text{Zone of Inhibition exhibited by test compound}}{\text{Zone of Inhibition by the refernce compound}}$$

The results are given in following table:

Table2. Antimicrobial Activity of 1,5-Benzothiazepine Derivatives

Compd	Series	Bacteria		Fungus
		S. aureus	*P. aeruginosa*	*C. albicans*
FS1	1	0 (0.00)	0 (0.00)	16 (1.14)
FS2	1	14 (0.63)	0 (0.00)	0 (0.00)
FS3	1	8 (0.37)	16 (0.67)	14 (1.00)
FS4	1	14 (0.63)	16 (0.67)	17 (1.21)
FS5	1	15 (0.68)	14 (0.58)	8 (0.57)
FS6	1	0 (0.00)	18 (0.75)	14 (1.00)
SS1	2	19 (0.95)	18 (1.00)	17 (1.21)
SS2	2	15 (0.75)	20 (1.11)	15 (1.07)
SS3	2	15 (0.75)	13 (0.72)	13 (0.92)
SS4	2	12 (0.60)	0 (0.00)	15 (1.07)
SS5	2	12 (0.60)	12 (0.67)	18 (1.28)
SS6	2	1 (0.50)	16 (0.89)	10 (0.71)
TS1	3	12 (0.54)	12 (0.50)	18 (1.28)
TS2	3	16 (0.72)	18 (0.75)	16 (1.14)
TS3	3	0 (0.00)	18 (0.75)	14 (1.00)
TS4	3	24 (1.09)	12 (0.50)	14 (1.00)
TS5	3	8 (0.36)	0 (0.00)	18 (1.28)
TS6	3	10 (0.45)	12 (0.50)	0 (0.00)
FO1	4	20 (0.90)	16 (0.67)	15 (1.07)
FO2	4	14 (0.63)	16 (0.67)	14 (1.00)
FO3	4	15 (0.68)	0 (0.00)	0 (0.00)
FO4	4	10 (0.45)	0 (0.00)	12 (0.85)
FO5	4	18 (0.81)	18 (0.75)	16 (1.14)
FO6	4	0 (0.00)	15 (0.62)	10 (0.71)

a. Zone of Inhibitions are given in mm, b. Values in parentheses represent activity index, c. Zone of Inhibition of Gatifloxin for *S. aureus* is 22 mm. d. Zone of Inhibition of Natilmicin for *P. aeruginosa* is 24 mm. e. Zone of Inhibition of Fluconazole for *C. albicans* is 14 mm, f. Concentration of test and reference compounds were 100µg/disc.

We tried to find out significant effect of different substituents on the yield obtained for the test compounds, to find out remarkable effect of substituents on the zone of inhibition and on activity index of the test compounds. Graphical analysis was firstly carried out on yield obtained from the different test compound given in the series 1st, 2nd, 3rd and 4th in the Table.1, under the influence of substituent-X and substituent-Z and then performed hypotheses testing using two-way and three-way ANOVA techniques with the help of SPSS.

[III] RESULTS AND DISCUSSION

The graphical analysis of yield obtained from the test compound:

Consider substituent–X as blocks and substituent-Z as treatments and substituent-Y is fixed. Following is the graphical representation of yield obtained from the different test compounds due to substituent-X and substituent-Z, which are mention in Table.1.

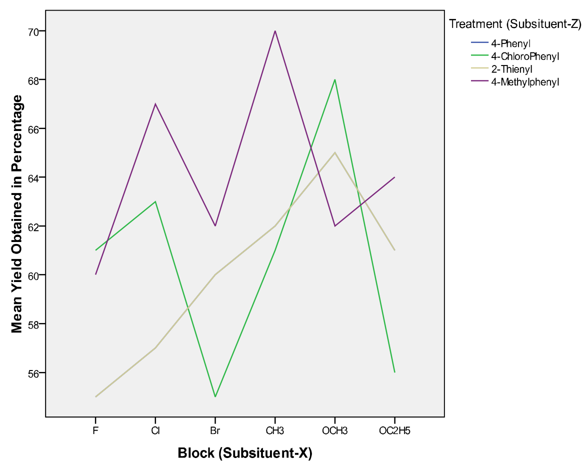

Fig. 2. The graphical representation of yield obtained from the test compounds due to substituent-X and substituent-Z

The graph shows that the yield obtained from the 2nd and 3rd series are equal for the respective compounds, i.e when there are 4-Phenyl and 2-Thienyl as substituent yield obtained from respective compound from series 2nd and 3rd are same.

Yield for compound SS1 and FO1 is almost same, also they are more than FS1 and TS1.Yield obtained from FO2 is highest in comparison of FS2, SS2 and TS2.Yield obtained from SS3 is lowest in comparison of FS3, TS3 and FO3, while these three have almost equal yield. Yield obtained from FO4 is highest among FS4, SS4 and TS4, while remaining three have almost equal yield. There is variation of 3-5% in the Yield obtained from the fifth compounds of all the series, though FS5 and TS5 have same yield. Compound SS6 obtained lowest yield and FO6 obtained highest yield among last compounds of the four series.

The hypotheses for yield obtained by the test compounds:

Consider following hypothesis for substituent-X:

H0: μX1=μX2=μX3=μX4=μX5=μX6, i.e., there is no significant difference between the effects of the substituent-X on the yield obtained from the test compounds.

H1: Atleast two of the means differ. There is significant difference between the effects of the atleast one of the substituent-X on the yield obtained from the test compounds.

Consider following hypothesis for substituent-Z:

H0: μZ1=μZ2=μZ3=μZ4, i.e., there is no significant difference between the effects of the substituent-Z on the yield obtained from the test compounds.

H1: Atleast two of the means differ, i.e., There is significant difference between effects of atleast one of the substituent-Z on the yield obtained from the test compounds.

We are testing the above hypotheses using two-way ANOVA techniques at 5% level of significance, to find out whether there is any significant difference between the effects of substituent-X and Substituent-Z on the yield of the compound. Following is the ANOVA (Analysis of variance) table obtained by SPSS to test the difference between the effects of Substituent-X and Substituent-Z on the yield obtained by the test compounds

Table 3. ANOVA (Analysis of variance) Table for the Yield Obtained by the Test Compounds

Tests of Between-Subjects Effects					
Dependent Variable: Yield Obtained in Percentage					
Source	**Type III Sum of Squares**	**df**	**Mean Square**	**F**	**Sig.**
X	148.708	5	29.742	2.763	.058
Z	71.792	3	23.931	2.223	.128
Error	161.458	15	10.764		
Total	90297.000	24			

From the above ANOVA table it is clear that significance is greater than 0.05 for both substituent-X and substituent-Z, therefore both the null hypotheses are not rejected. Hence there is no significant difference between the effects due to substituent-X on the yield obtained from the test compound. Also there is no significant difference between the effects due to substituent-Z on the yield obtained from the test compound.

The hypotheses for the zone of the inhibition exhibited by the test compounds:

Consider following hypothesis for substituent-X:

H0: μX1=μX2=μX3=μX4=μX5=μX6, i.e., there is no significant difference between the effect of the substituent-X on the zone of inhibition exhibited by test compounds.

H1: Atleast two of the means differ, i.e., there is significant difference between the effect of atleast one of the substituent-X on the zone of inhibition exhibited by test compounds.

Consider following hypothesis for substituent-Z

H0: μZ1=μZ2=μZ3=μZ4, i.e., there is no significant difference between the effect of the substituent-Z on the zone of inhibition exhibited by test compounds.

H1: Atleast two of the means differ, i.e., there is significant difference between the effect of atleast one of the substituent-Z on the zone of inhibition exhibited by test compounds.

Consider following hypothesis for Microbes:

H0: μM1=μM2=μM3, i.e., there is no significant difference between the effect of the microbes on the zone of inhibition exhibited by test compounds.

H1: Atleast two of the means differ, i.e., there is significant difference between the effect of atleast one of the Microbes on the zone of inhibition exhibited by test compounds.

We are testing the above hypotheses using three-way ANOVA techniques at 5% level of significance, to find out the whether there is any significant difference between the effect due to substituent-X, substituent-Z and microbes on the zone of inhibition exhibited by test compound.

Following is the ANOVA (Analysis of variance) Table which is obtained by using SPSS:

Table 4. ANOVA (Analysis of variance) Table for the Zone of Inhibition exhibited by Test Compounds

Tests of Between-Subjects Effects					
Dependent Variable: Zone of inhibition exhibited by test compound					
Source	**Type III Sum of Squares**	**df**	**Mean Square**	**F**	**Sig.**
X	340.236	5	68.047	1.724	.143
Microbes	15.361	2	7.681	.195	.824
Z	125.819	3	41.940	1.063	.372
Error	2407.569	61	39.468		
Total	13281.000	72			

It is clear from the ANOVA table that significance for all the three components is more than 0.05, therefore all the three null hypotheses are not rejected. That is there is no significance difference between the effects of Substituent-X, Substituent-Z and Microbes on the zone of inhibition exhibited by test compounds.

The hypotheses for activity index of the test compounds

Consider following hypothesis for substituent-X:

H0: μX1=μX2=μX3=μX4=μX5=μX6, i.e., there is no significant difference between the effects of the substituent-X on the activity index of the test compounds.

H1: Atleast two of the means differ, i.e., there is no significant difference between the effects of the substituent-X on the activity index of the test compounds.

Consider following hypothesis for substituent-Z:

H0: μZ1=μZ2=μZ3=μZ4, i.e., there is no significant difference between the effect of the substituent-Z on the activity index of the test compounds.

H1: Atleast two of the means differ, i.e., there is significant difference between the effects of the substituent-Z on the activity index of the test compounds.

Consider following hypothesis for microbes:

H0: μM1=μM2=μM3, i.e., there is no significant difference between the effects of the microbes on the activity index of the test compounds.

H1: Atleast two of the means differ, i.e., there is significant difference between the effects of atleast one of the microbes on the activity index of the test compounds.

We are testing the above hypotheses using three-way ANOVA techniques at 5% level of significance, to find out the whether there is any significant difference between the effects of substituent-X, substituent-Z and microbes on the activity index of test compound. Following is the ANOVA (Analysis of variance) Table which is obtained by using SPSS:

Table 5. ANOVA (Analysis of Variance) Table for Activity Index of the Test Compounds.

Tests of Between-Subjects Effects					
Dependent Variable: Activity Index of test compounds					
Source	**Type III Sum of Squares**	**df**	**Mean Square**	**F**	**Sig.**
X	.984	5	.197	1.805	.125
Microbes	2.114	2	1.057	9.700	.000
Z	.740	3	.247	2.262	.090
Error	6.648	61	.109		
Total	41.836	72			

It is clear from the ANOVA table that the significance for substituent-X and substituent-Z is more than 0.05, therefore null hypotheses for both the substituent are accepted, i.e., there no significant difference between the effects of both the substituent on the Activity Index of the test compounds.

But, significance for Microbes is less than 0.05, therefore null hypothesis for microbes is rejected. Hence there is significance difference between the effects of microbes on the activity index of the test compounds at 5% level of significance.

For further analysis, the effects of two microbes on the activity index are compared. For this, first *Staphylococcus aureus* and *Pseudomonas aeruginosa* are taken.

Consider following hypothesis for microbes:

H0: μM1=μM2, i.e., there is no significant difference between the effects of two microbes on the activity index of the test compounds.

H1: μM1≠μM2, i.e., there is significant difference between the effects of two microbes on the activity index of the test compound.

The ANOVA table obtained from SPSS for the effect of these microbes on activity Index of the test compounds is as follows:

Table 6. ANOVA Table for Activity index of the Test Compounds with Bacteria (*Staphylococcus aureus* & *Pseudomonas aeruginosa*)

Tests of Between-Subjects Effects					
Dependent Variable: Activity index of the test compound					
Source	**Type III Sum of Squares**	**df**	**Mean Square**	**F**	**Sig.**
X	.619	5	.124	1.291	.288
Microbes	.002	1	.002	.022	.882
Z	.557	3	.186	1.935	.140
Error	3.646	38	.096		
Total	18.757	48			

From the Table 6, it is clear that at 5% level of significance, null hypothesis is not rejected as significance for microbes is more than 0.05, this implies there is no significant difference between the effects of these bacteria (*Staphylococcus aureus* and *Pseudomonas aeruginosa*) on the Activity Index of the test compound.

Now taking the bacteria, *Staphylococcus aureus* and Fungus, *Candida albicans* for the comparison.

Consider following hypothesis for microbes:

H0: μM1=μM3, i.e., there is no significant difference between the effects of two microbes on the activity index of the test compounds.

H1: μM1≠μM3, i.e., there is significant difference between the effects of two microbes on the activity index of the test compound.

The ANOVA table is obtained for the effects of microbes (*Staphylococcus Aureus* and Fungus, *Candida Albicans*) on the Activity Index of the test compound, is as follows:

Table 7. ANOVA Table for Activity Index of the test compound (*Staphylococcus aureus* and Fungus, *Candida albicans*)

Tests of Between-Subjects Effects					
Dependent Variable: Activity Index of the test compound					
Source	**Type III Sum of Squares**	**df**	**Mean Square**	**F**	**Sig.**
X	.584	5	.117	.865	.514
Z	.541	3	.180	1.333	.278
Microbes	1.643	1	1.643	12.152	.001
Error	5.137	38	.135		
Total	32.587	48			

From the Table **7**, it is found that significance for microbes is less than 0.05, so null hypothesis is rejected at 5% level of significance, this implies that there is significant difference between the effects of *Staphylococcus aureus* and Fungus *Candida albicans* on the activity Index of the test compound. At last taking the microbes *Pseudomonas aeruginosa* and Fungus, *Candida albicans* for the comparison.

Consider following hypothesis for microbes:

H0: μM2=μM3, i.e., there is no significant difference between the effects of two microbes on the activity index of the test compounds.

H1: μM2≠μM3, i.e., there is significant difference between the effects of two microbes on the activity index of the test compound.

When the effect of *Pseudomonas aeruginosa* and Fungus, *Candida albicans* is compared on the activity index of the test compound, following ANOVA table is obtained:

Table 8. ANOVA Table for Activity Index of the test compound (*Pseudomonas aeruginosa* and Fungus, *Candida albicans*).

Tests of Between-Subjects Effects					
Dependent Variable: Ratio of Zone of Inhibited by test Compound and Zone of Inbition exhibited by the reference compound					
Source	**Type III Sum of Squares**	**df**	**Mean Square**	**F**	**Sig.**
X	1.351	5	.270	2.658	.037
Z	.443	3	.148	1.454	.242
Microb	1.527	1	1.527	15.016	.000
Error	3.863	38	.102		
Total	32.328	48			

It is clear from Table **8**, that here also the significance for microbes is less than 0.05, therefore null hypothesis is rejected at 5% level of significance. This implies that there is significant difference between the effects of *Pseudomonas aeruginosa* and Fungus, *Candida albicans* on the activity index of the test compound.

Hence, from above analysis it is found that the effect of Fungus, *Candida albicans* is significantly different from the effect of other two microbes on the Activity Index of the test compound.

CONCLUSIONS

As per the results, obtained from analysis of variance (ANOVA) from table 3-table 8 it is found that, there is no significant difference between the effect of X-Substituents i.e. F, Cl, Br, CH_3, OCH_3, OC_2H_5 and Z-substituents i.e. phenyl, 4-chlorophenyl, 2-thienyl, 4-methyl phenyl on yield of compounds and on zone of inhibition of microbes. However, microbes have significant difference between the effects on the activity index of the test compounds. On further analysis, it was found that the effects of fungus *Candida albicans* is significantly different then the effects of other two bacteria on the Activity Index of the test compound.

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REFERENCES

1. Dandia, A., Ruby, S., Dharmendra, S., Ashok, L. & Asha, S., (2010), Regioselective synthesis of diltiazem analogue pyrazolo[4,3-c][1,5] benzothiazepines and antifungal activity, Phosphorus, Sulfur, Silicon & Related Elements, 185, 2472.
2. Desai, K.G. & Desai, K.R., (2007), Microwave enhanced heterocyclization: A convenient procedure for antimicrobial 1,5-benzothiazepine compounds. Indian Journal of Chemistry, Sect. B, 46B, 1179.
3. Ghotekar, D.S., Joshi, R.S., Mandhane, P.G., Bhagat, S.S. & Gill, C.H., (2010), Synthesis of some biologically important fluorinated 3-chlorochromones and 1,5-benzothiazepines as antimicrobial and antifungal agents, Indian Journal of Chemistry, Sect. B, 49B, 1267.
4. Garg, N., Chandra, T., Jain, A., Jain, A.B. & Kumar, A., (2010), Synthesis and evaluation of some new substituted benzothiazepine and benzoxazepine derivatives as anticonvulsant agents, European Journal of Medicinal Chemistry, 45, 1529.
5. Grandolini, G., Perioli, L. & Ambrogi, V., (1999), Synthesis of some new 1,4-benzothiazine and 1,5-benzothiazepine tricyclic derivatives with structural analogy with TIBO and their screening for anti-HIV activity, European Journal of Medicinal Chemistry, 34, 701.
6. Pant, S., Sharma, P. & Pant, U.C., (2008), Syntheses of 1,5-Benzothiazepines: Part XXXVI- Syntheses and antimicrobial studies of 8-substituted-2-(2-chlorophenyl)-2,5-dihydro-4-(4-chlorophenyl/2-thienyl)-1,5-benzothiaze-pines, Phosphorus, Sulfur, Silicon & Related Elements, 183, 2974.
7. Pant, S., Singhal, B., Upreti, M. & Pant, U. C., (1998), Syntheses of 1, 5-Benzothiazepines. Part 20. Syntheses of 8-Substituted-2,5-dihydro-2-(4-N-dimethylaminophenyl)-4-(4-methoxyphenyl)-1,5-benzothiazepines**,** Molecules, 3, 159.
8. Pant, S., Sharma, P., Sharma, B. S. & Pant, U. C., (2007), Syntheses of 1,5-Benzothiazepines: Part XXXIII–Syntheses of 10-substituted-6a,7-dihydro-6-(4-methoxyphenyl)-7-(4-methoxy-phenyl/3,4-dimethxoyphenyl)-6H[1]benzo-pyrano[3,4-

c][1,5]benzothiazepines, Indian Journal of Chemistry, 46B, 1537.

9. Pant, S., Chandra, H., Sharma, P. & Pant, U. C., (2006), Syntheses of 1,5-Benzothiazepines: Part XXIX-Syntheses of 10-substituted-6a,7-dihydro-6H-7-(4-ethoxyphenyl)-6-phenyl[1] benzopyrano[3,4-c][1,5]benzothiazepines, Indian Journal of Heterocyclic Chemistry, 15, 289.
10. Pant, S., Sharma, P., Sharma, B. S. & Pant U. C., (2007), Syntheses of 1,5-Benzothiazepines: Part XXXIII–Syntheses of 10-substituted-6a,7-dihydro-6-(4-methoxyphenyl)-7-(4-methoxy-phenyl/3,4-dimethxoyphenyl)-6H[1]benzo-pyrano[3,4-*c*][1,5] benzothiazepines, Indian Journal of Chemistry, 46B, 1537.
11. Pant, S., Sharma, P. & Deepika, (2009), Syntheses of 1,5-Benzothiazepines: Part XXXVII- Syntheses and antimicrobial evaluation of 8-substituted-2,5-dihydro-2-(4-methoxyphenyl/3,4-dimethoxyphenyl)-4-phenyl-1,5-benzothiazepines, Indian Journal of Heterocyclic Chemistry, 19, 5.
12. Pant, S., Sharma, P. & Jadon, R., (2012), Syntheses of 1,5-benzothiazepines: Part XXXVIII - Syntheses and antimicrobial evaluation of bicyclic 8-substituted-2,5-dihydro-2,4-diaryl-1,5-benzothiazepines and tetracyclic 10-substituted-6,7-diaryl-6a,7-dihydro-6*H*[1]benzopyrano [3,4-c][1,5] benzothiazepines, Indian Journal of Heterocyclic Chemistry, 21, 341.
13. Pant, S., Sharma, P., Sharma, A. Mishra, R. & Pant, U. C., (2008), Syntheses of 1,5-Benzothiazepines: Part XXXIV- Syntheses and antimicrobial studies of 8-substituted-2-(4-methoxyphenyl/3,4-dimethoxyphenyl)-2,5-dihydro-4-(2-thienyl)-1,5-benzothiazepines, Journal of Indian Chemical Society, 85, 406-411.
14. Sharma, P. & Pant, S., (2014), Syntheses and antimicrobial evaluation of bicyclic 8-substituted-2,5-dihydro-2-(3,4-dimethoxy-phenyl)-4-(4-methylphenyl)-1,5-benzothiaze-pines, International Journal of Chemical Sciences & Applications, 5(1), 7.
15. Pant, U. C., Upreti, M., Pant, S., Dandia, A., Patnaik, G.K. & Goel, A. K., (1997), Syntheses of 1,5-benzothiazepines, part xvi: syntheses of 8-ethoxy/fluoro-2-caboxy-4-(fluorinated aryl) -2,3dihydro1,5-benzothiazepinesas prospective cardiovascular agents, Phosphorous, Sulfur, Silicon & Related Elements, 126, 193.
16. Saini, R.K., Joshi, Y.C. & Joshi, P., (2008), Solvent-free synthesis of some 1,5-benzothiazepines and benzodiazepines and their antibacterial activity, Phosphorus, Sulfur, Silicon & Related Elements, 183, 2181.
17. Sarro, G.D. Chimirri, A., Sarro, A.D., Gitto, R. & Grasso, S. Zappala. (1995), 5*H*-[1,2,4]Oxadiazolo[5,4-*d*][1,5] benzothiazepines as anticonvulsant agents in DBA/2 mice, European Journal of Medicinal Chemistry, 30, 925.