"Green Synthesis of Promising Antimicrobial N-Substituted Chromene Aryl Sulfonamide Scaffolds Using Green Fe@Si-IL Catalyst"

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INTRODUCTION

➢ Numerous pathogenic bacteria occur in nature but the available antibacterial agents or antibiotics have limited inhibitory or killing action on bacteria.

➢Antibacterial agents/Antibiotics are used to kill or control the growth of pathogenic bacteria. Still, with the long-term usage of an antibacterial agent, there are chances that bacteria develop resistance against antibacterial/antibiotics.

➢Sulfonamide derivatives containing thiophene and chromene moieties have diverse biological activities So the requirement of the new group of antibacterial compounds.

OBJECTIVE

➢ The aim of the present study is to tap the potential of heterocyclic and aryl sulfonamide classes.

➢ Synthesis of N-substituted aryl sulfonamide containing chromene moieties.

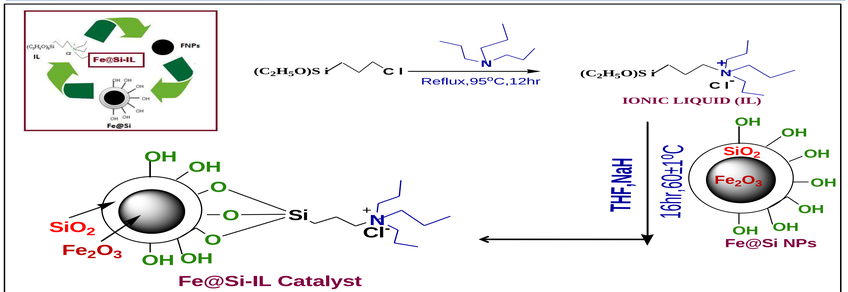
➢. Structural elucidation of synthesized compounds by using techniques like NMR, IR, and UV-VIS spectroscopy.

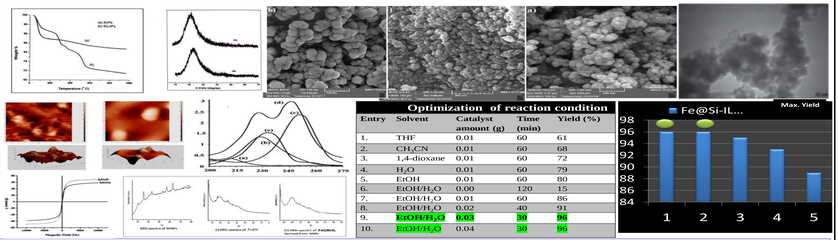
➢ Evaluation of the antibacterial activity of synthesized compounds

MATERIAL AND METHODS

➢The magnetic ferrite nanoparticles (FNP) were synthesized by treating several concentration of $FeCl_2.4H_2O$ with ammonia solution at 80±1°C.

➢FNPs were coated with SiO_2 followed by reaction with ionic liquid to develop magnetic nano ionic capsule Fe@Si-IL at 16 hr, 80±1°C





Optimization of reaction condition				
Entry	Solvent	Catalyst amount (g)	Time (min)	Yield (%)
1.	THF	0.01	60	61
2.	CH_3CN	0.01	60	68
3.	1,4-dioxane	0.01	60	72
4.	H_2O	0.01	60	79
5.	EtOH	0.01	60	80
6.	EtOH/H_2O	0.00	120	15
7.	EtOH/H_2O	0.01	60	86
8.	EtOH/H_2O	0.02	40	91
9.	EtOH/H_2O	0.03	30	96
10.	EtOH/H_2O	0.04	30	96

Fig.1.1 Schematic Surface Futionalisation of a Ionic liquid attached with SiO_2 coated on ferrites nanoparticles (Fe_2O_3).

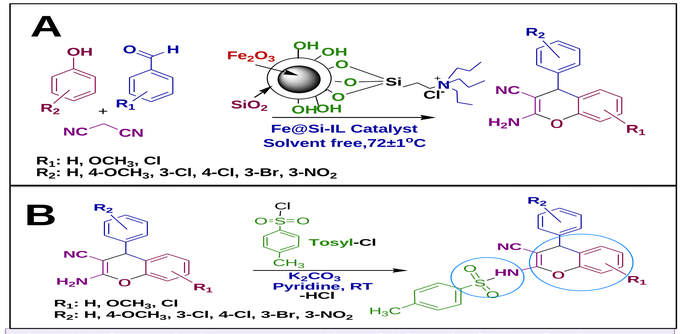
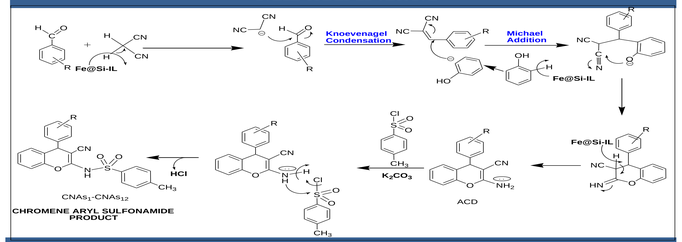


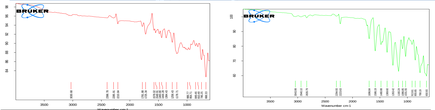
Fig.1.2 Schematic Representation of Chemical Synthesis

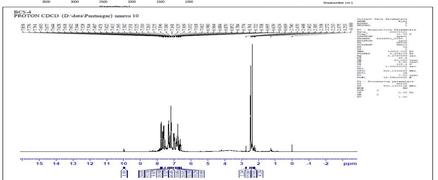
MECHANISM



RESULT

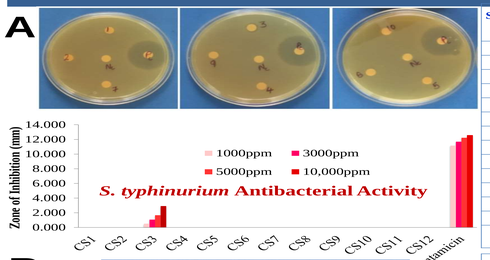
Structure	Abbreviation	Yield (%)	M.P (°C)	Colour
1.	$CNAS_1$ (-H)	81.09	99-105	Cream
2.	$CNAS_2$ (3-OCH_3)	83.33	97-102	Light Brown
3.	$CNAS_3$ (2-Cl)	77.40	107-115	Cream White
4.	$CNAS_4$ (3-Cl)	78.80	99-106	White
5.	$CNAS_5$ (4-Cl)	49.02	93-104	Reddish Brown
6.	$CNAS_6$ (3-Br)	44.69	69-88	Dark Yellow
7.	$CNAS_7$ (4-F)	58.09	99-116	Off-White
8.	$CNAS_8$ (3-OH)	75.11	115-130	Dark Brown
9.	$CNAS_9$ (4-OH)	70.81	117-128	Cream
10.	$CNAS_{10}$ (4-NO_2)	61.07	127-136	Pale Yellow
11.	$CNAS_{11}$ (2,3-di Cl)	32.41	87-105	Dark Brown
12.	$CNAS_{12}$ (3,4-di OCH_3)	67.81	136-143	Orange



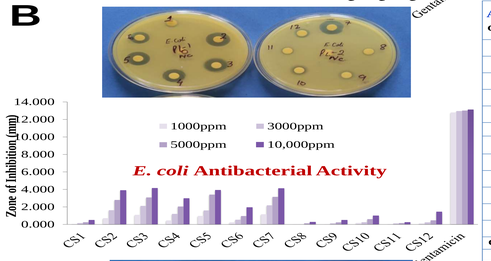


- **UV-vis:** 258.40 nm,
- **IR (KBr):** 2210.84 cm^{-1} (CN), 3030.68 cm^{-1}(NH), 1364.43 cm^{-1}, 1178.71 cm^{-1} (S=O), 1549.91 cm^{-1} (C=C aromatic).
- **NMR (400MHz, $CDCl_3$) δ(ppm):** 2.43 ppm (s, 3H), 2.14 ppm (s,1H), 7.77 ppm (s, 1H, NH-SO_2), 7.68 ppm (d, J = 8Hz, 2H), 6.95 ppm (d, J = 8Hz, 2H), 7.62-7.99 ppm (m, 5H, C-H_{Ar}), 7.19-7.30 ppm (m, 4H, C-H_{Ar}).

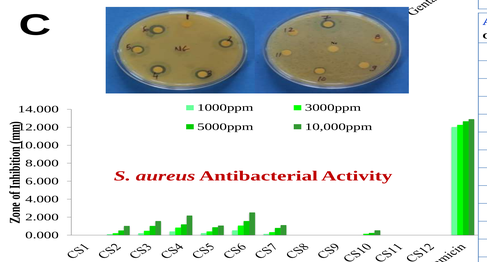
ANTI-BACTERIAL AGENT



Statistical Analysis	*S. typhinurium*				
Compounds	1000ppm	3000ppm	5000ppm	10,000ppm	CD at 5%
CS_1	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
CS_2	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
CS_3	**0.517±0.029**	**1.067±0.115**	**1.667±0.289**	**2.900±0.173**	**0.201**
CS_4	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
CS_5	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
CS_6	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
CS_7	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
CS_8	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
CS_9	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
CS_{10}	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
CS_{11}	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
CS_{12}	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
Gentamicin	**11.163±0.048**	**11.690±0.093**	**12.225±0.046**	**12.583±0.083**	**0.135**
CD at 5%	0.046	0.059	0.022	0.090	



Analysis	*E. Coli*				
Compounds	1000ppm	3000ppm	5000ppm	10,000ppm	CD at 5%
CS_1	**0.051±0.001**	**0.151±0.001**	**0.257±0.011**	**0.513±0.012**	**0.015**
CS_2	0.710±0.036	1.633±0.076	2.800±0.050	3.900±0.087	0.125
CS_3	1.093±0.040	2.117±0.029	3.083±0.076	4.167±0.144	0.163
CS_4	0.454±0.132	1.202±0.134	2.050±0.132	2.983±0.029	0.221
CS_5	0.969±0.073	1.600±0.132	3.417±0.382	3.917±0.144	0.416
CS_6	0.238±0.029	0.537±0.028	0.953±0.048	1.935±0.056	0.080
CS_7	1.158±0.070	2.185±0.020	3.153±0.130	4.137±0.118	0.182
CS_8	0.002±0.002	0.025±0.022	0.135±0.030	0.262±0.020	0.041
CS_9	0.007±0.003	0.135±0.013	0.243±0.012	0.517±0.029	0.032
CS_{10}	0.165±0.005	0.252±0.003	0.602±0.088	1.002±0.048	0.096
CS_{11}	0.036±0.005	0.120±0.017	0.156±0.011	0.255±0.005	0.020
CS_{12}	0.114±0.008	0.233±0.029	0.467±0.202	1.433±0.161	0.248
Gentamicin	12.789±0.014	12.960±0.055	13.017±0.029	13.128±0.129	0.138
CD at 5%	0.083	0.103	0.230	0.158	



Analysis	*S. aureus*				
Compounds	1000ppm	3000ppm	5000ppm	10,000ppm	CD at 5%
CS_1	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
CS_2	0.121±0.027	0.220±0.026	0.520±0.026	1.033±0.029	0.052
CS_3	0.222±0.025	0.485±0.030	1.035±0.030	1.568±0.079	0.089
CS_4	0.423±0.025	0.842±0.019	1.202±0.148	2.183±0.161	0.211
CS_5	0.228±0.020	0.425±0.025	0.890±0.036	1.067±0.058	0.072
CS_6	0.535±0.026	1.067±0.076	1.567±0.076	2.533±0.029	0.110
CS_7	0.136±0.027	0.335±0.026	0.800±0.050	1.118±0.076	0.094
CS_8	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
CS_9	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
CS_{10}	0.007±0.005	0.161±0.012	0.254±0.003	0.537±0.033	0.034
CS_{11}	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
CS_{12}	0.000±0.000	0.000±0.000	0.000±0.000	0.000±0.000	-
Gentamicin	12.033±0.029	12.265±0.125	12.663±0.031	12.901±0.076	0.146
CD at 5%	0.032	0.074	0.086	0.104	

CONCLUSION

➢ The Synthesis of chromene moiety containing aryl sulfonamides was prepared in two steps to afford final products (CNAS1-CNAS12) with good to excellent yield. At 10,00ppm, CNAS3 exhibited maximum inhibition against E.coli (4.167mm) as compared to S. typhinurium (CNAS3 -2.900mm) and S. aureus (CNAS6 -2.533mm).

➢Synthesized compounds were found to have significantly lower antibacterial activity than the standard Gentamicin but at a concentration of 10,00ppm, some derivatives of three different classes exhibited good activity.

➢Synthesized green nanomagnetic ionic catalyst. Fe@Si-IL could be extracted easily by using a magnetic separation method and can be used rapidly without loss of catalyst properties..

REFERENCES

➢ S. Beiranvand, A. Eatemadi, A. Karimi, *Nanoscale Res Lett* **2016**, 11:307.

➢A. Rueda-Zubiaurre, S. Yahiya, O. J. Fischer, X. Hu, C. N. Saunders, S. Sharma, and J. Baum, *Journal of medicinal chemistry*, **2019** *63*(5), 2240-2262.

➢Li, Q. Z., Nie, X. Y., & Liang, J. *Letters in Drug Design & Discovery*, **2011** *8*(6), 558-561.