SYNTHESIS AND ANTIBACTERIAL ACTIVITY EVALUATION OF CARBAZOLE-BASED COMPOUNDS

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Even though there are many antibacterial agents multidrug resistant bacteria poses a huge threat to public health and has become one of the biggest health problems in the last decade. Therefore, there is an urgent need to develop and provide novel and more potent antibacterial agents to overcome drug resistance [1].

Carbazole is a nitrogen containing aromatic heterocyclic compound, which can be found in nature as carbazole alkaloid that is isolated from various part of the plan [2]. Such carbazole ring containing alkaloids are carbomycins that were first isolated from *Streptoverticillium ehimense* and showed good activity against various organisms, which made carbazoles a desirable target for further biological research [3].

It has been observed that carbazole compounds exhibit multiple mechanisms of antibacterial activity action. One is that carbazole compounds increase membrane permeability by inhibiting specific enzymatic processes. Increased penetration of free radicals in violates integrity of bacterial cell [4]. Second, mechanism of action is that carbazole compounds can interact with bacterial DNA by forming non-covalent interactions with DNA gyrase [5]. Therefore, various N and C substituted carbazoles are attractive target to develop and produce new antibacterial agents with two possible antibacterial mechanism of action, that could help resolve drug resistance problem.

In this work, various mono-, di- and tri-substituted carbazole derivatives, containing appropriate halogens, cyano and alkyl groups were synthesized and evaluated for their antibacterial activities against two bacteria (*Bacillus subtilis* and *Escherichia coli*) using disk diffusion method. Screening of their antibacterial activity has displayed that against *Bacillus subtilis* the most active antibacterial agents 3-cyano-9*H*-carbazole, 3-iodo-9*H*-carbazole and 3,6-diiodo-9*H*-carbazole, they suppressed the growth of bacteria at concentration 31.25 μg ml^{-1}. *Escherichia coli* bacteria was the most sensitive to 1,3,6-tribromo-9*H*-carbazole, which inhibited their growth at concentration of 31.25 μg ml^{-1}.

Antioxidative activities were evaluated using free 1,1-diphenyl-2-picryl-hydrazyl radical scavenging assay and ferric reducing antioxidant power methods. Antioxidant activity assay revealed that tested compounds displayed from none to very weak antioxidant activity according to tested methods.

Table 1. The antibacterial activity results against *Bacillus subtilis* and *Escherichia coli* strains of selected compounds 1a-5 at different concentrations**.**

Strain		*Bacillus subtilis*				*Escherichia coli*			
Concentration (μg ml^{-1})		1000	125	62.5	31.25	1000	125	62.5	31.25
Zone of inhibition (mm)	**1a**	10.5	8.0	7.9	5.3	10.45	6.30	NA	NA
	1b	9.50	NA	NA	NA	9.67	NA	NA	NA
	2a	8.00	7.95	8.20	5.47	10.20	8.60	6.17	NA
	2b	9.00	7.18	7.20	6.33	10.20	9.65	6.00	NA
	3	10.30	7.68	7.40	NA	9.67	8.70	7.67	5.95
	4	8.50	7.15	NA	NA	7.75	NA	NA	NA
	5	NA	NA	NA	NA	NA	NA	NA	NA

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