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ANTIBACTERIAL ACTIVITY OF S, N-DISUBSTITUTED QUINAZOLINES

Z.A. HOVASYAN, S.H. POGHOSYAN, M.R. HAKOBYAN*, H.M. STEPANYAN, R.E. MURADYAN, A.A. HARUTYUNYAN

Scientific and Technological Center of Organic and Pharmaceutical Chemistry of NAS RA, marinehakobyan88@mail.ru

Melting points, IR spectral data, and results of studying the antibacterial activity of new synthesized 2,3-disubstituted quinazolin-4(3*H*)-ones are presented. The antibacterial properties of quinazolines were studied against four strains of gram-positive and gram-negative bacteria.

2,3-disubstituted quinazolin-4(3H)-ones – physical data – antibacterial properties

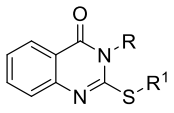
Ներկայացված են հալման կետերը, IR սպեկտրային տվյալները և նոր սինթեզված 2,3-դիփոխարինված քինազոլին-4(3H)-երի հակաբակտերիալ ակտիվության ուսումնասիրության արդյունքները: Ուսումնասիրվել են քինազոլինների հակաբակտերիալ հատկությունները գրամ դրական և գրամ-բացասական բակտերիաների չորս շտամների նկատմամբ:

2,3-էփոխարինված քինազոլին-4(3H)-ոններ – ֆիզիկական տվյալներ – հակաբակտերիալ հատկություններ

Приведены точки плавления, данные ИК-спектров и результаты изучения антибактериальной активности новых синтезированных 2,3-дизамещенных хиназолин -4(3*H*)-онов. Изучены антибактериальные свойства хиназолинов в отношении четырех штаммов грамположительных и грамотрицательных бактерий.

2,3-дизамещенные хиназолин-4(3H)-оны – физические данные – антибактериальные свойства

It is known that derivatives of 2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one and its S, N-disubstituted derivatives exhibit significant biological activity [4]. In continuation of research on the synthesis of quinazoline derivatives [3], we obtained various S, N-disubstituted quinazolines and studied their antibacterial properties against strains of gram-positive and gram-negative bacteria (fig.1).



1a-n

R,R^1 = Et, $CH_2C(O)$-3-ClC_6H_4 (**a**), *cyclo*-C_6H_{11}, Pr (**b**), *cyclo*-C_6H_{11}, Bu (**c**), *cyclo*-C_6H_{11}, CH_2CN (**d**), *cyclo*-C_6H_{11}, $CH_2C{\equiv}CH$ (**e**), CH_2*cyclo*-C_6H_{11}, Me (**f**), CH_2*cyclo*-C_5H_9, CH_2-3-ClC_6H_4 (**g**), Ph, Bu (**h**), Ph, $CH_2CH{=}CH_2$ (**i**), Ph, CH_2CH_2Ph (**j**), Ph, $CH_2C(O)$-3-ClC_6H_4 (**k**), 2-MeC_6H_4, Pr (**l**), CH_2Ph, Bu (**m**), CH_2Ph, CH_2COOEt (**n**).

Compounds **1a-n** were synthesized by alkaline alkylation of 3-alkyl(aryl)-substituted 2-thioxoquinazolin-4(3*H*)-ones, which, in turn, were obtained by the reaction of anthranilic acid with the corresponding isothiocyanates according to known methods [1].

Materials and methods. The antibacterial activity of the compounds was studied by the methods of "diffusion in agar" using the described method [2]. In the experiments, standard reference strains of microorganisms were used: two strains of gram-positive staphylococcus (*Staphylococcus aureus 209p and S. aureus 1*) and gram-negative rods (*Shigella flexneri 6858, Esherichia coli 0-55*) differing in sensitivity to antibacterial drugs.

Table 1. Melting points, IR-spectra data and antibacterial activity of compounds 1a-n and ontrol antibacterial drug furazolidone (F)

Compounds	M.p.,ºC	IR-spectra: CO, CH=N, CH=CH	The diameter of the zone of no microbial growth (mm)*			
			St.aureus 209 p	Bac.subtilis	Sh. flexneri	E.coli 0-55
1a	170-172	1695,1683, 1607	10	14	10	12
1b	68-70	1686,1663, 1611	17	16	15	16
1c	64-66	1686,1609	15	16	10	13
1d	118-119	2250 (CN), 1683,1606	0	0	0	0
1e	182-184	3246(≡CH),1678, 1604	14	15	13	15
1f	79-80	1676, 1607	17	17	12	10
1g	166-168	1682,1669,1605	15	14	15	12
1h	110-112	1692,1605	15	10	0	0
1i	148-150	1672,1636,1603	0	0	0	0
1j	118-120	1687,1606	10	12	10	13
1k	207-209	1681,1605	15	15	15	10
1l	70-72	1681,1608	10	14	0	13
1m	59-61	1681,1604	10	15	15	15
1n	104-106	1736,1685,1608	10	15	15	10
F	------	-------	25	24	24	24

Results and Discussion. It has been established that the majority of the studied pyrimidines exhibit weak antibacterial properties with respect to all test strains. At the same time, the combination of two hydrophobic groups in 3-cyclohexyl-2-propyl(butyl)thioquinazolin-4(3*H*)-ones **1b,c,e** leads to some enhancement of antibacterial properties, which disappear when the alkyl groups at the sulfur atom are replaced by a polar one cyanomethyl group in compound 1d. Note that the replacement of the cyclohexyl group with cyclopentyl and cyclohexylmethyl groups in position 3 of the ring and the preservation of the hydrophobic nature of the substituent in position 2 of the quinazoline ring in compounds 1f, g, i,e, the introduction of a methylene link between the quinazoline and cycloalkane fragments, does not affect the level of antibacterial activity of the compounds. The antibacterial activity of quinazoline derivatives 1i-n with aromatic groups in positions 3 of the quinazoline ring is less

pronounced. Thus, in the series of synthesized 2,3-disubstituted quinazolines, derivatives with cycloalkyl groups in position 3 of the quinazoline ring show a certain antibacterial activity, while at the same time significantly yielding to the control drug furazolidone.

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