in Table I and equation (1) the values of $(K' - K'')$ and K'' can be obtained by the method of least squares.

TABLE I

$[S_2O_8] = 1 \cdot 0 \times 10^{-2}$ M $\quad [Ag^+] = 7 \cdot 70 \times 10^{-4}$ M
Temp. = 35° C.

pH	$[L^-]$	[HL]	α	$k_1 \times 10^2$ min.$^{-1}$	$K = k_1/[Ag^+]$
3·98	0·04	0·03	0·572	1·49	19·35
3·73	0·03	0·04	0·429	1·35	17·53
3·46	0·02	0·05	0·286	1·28	16·49
3·03	0·01	0·06	0·143	1·07	13·90

Calculations, show that the value of $(K' - K'') = 12 \cdot 29$ and $K'' = 12 \cdot 48$ litre mole^{-1} min.$^{-1}$ This gives $K' = 24 \cdot 77$ litre mole^{-1} min.$^{-1}$

This shows that the specific rate constant of lactate is nearly twice that of undissociated lactic acid.

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University of Udaipur, G. V. BAKORE.
Udaipur, *December* 30, 1967.

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SOME NEW POTENTIAL ANTITUBERCULARS: BENZOTHIAZOLYL GUANIDINES

THE antimalarial activity exhibited by some substituted diguanides[1] stimulated the search for other therapeutically useful members of this series and in due course led to the discovery of high antibacterial activity[2] and antitubercular activity,[3] especially among a series of *bis*-diguanides. Biguanido derivatives[3,4] of diaryl sulphones and sulphides have been found to exhibit antitubercular activity against *Myco. tuberculosis* in *in vitro* tests. In order to determine the degree of molecular complexity necessary for high antimicrobial potency, the stepwise synthesis of polyguanidines was undertaken and it was seen that antitubercular activity was highest in *bis*-diguanides in which the terminal groups were aryl, alkyl or heterocyclic nucleus.

Recently, Bhargava *et al.*[5,6] have synthesised several N-aryl-N'-2-(substituted) benzothiazolyl guanidines and have shown that the hydrochlorides of these bases are more active against gram-positive bacteria as compared with the gram-negative ones. The above findings led the authors to synthesise some new N - *m* - tolyl- N' - 2 - (substituted) benzothiazolyl–N"–alkyl guanidines as potential antituberculars.

In the present communication, 2-amino-(substituted) benzothiazoles[7,8] were condensed with *m*-tolylisothiocyanate. The resulting benzothiazolylthiocarbamides[9] were desulphurised with yellow lead oxide and various ethanolic alkylamines to give corresponding guanidines.

EXPERIMENTAL

N - m - tolyl - N' - 2 - (6-chloro) benzothiazolyl-N"-methyl guanidine.—N-*m*-tolyl-N'-2-(6-chloro) benzothiazolyl thiocarbamide (3·3 g.), yellow lead oxide (4 g.), ethanolic methyl amine (20 ml.) were heated in a glass autoclave on a water-bath for 3 hours. After cooling, the autoclave was opened carefully, and the product was boiled with ethanol (60 ml.) and filtered hot. The filtrate on cooling gave beautiful crystals. It was recrystallised from ethanol.

Similarly, other N-*m*-tolyl-N'-2-(substituted) benzothiazolyl–N"–alkyl guanidines have been prepared using different alkylamines. The yields, melting point and analytical data of N - *m* - tolyl - N' - 2 - (substituted) benzothiazolyl-N"-methyl guanidines and N-*m*-tolyl-N'-2-(substituted) benzothiazolyl-N"-ethyl guanidines are listed in Tables I and II.

Besides these, the yields, melting points and analytical data of N-*m*-tolyl-N'-2-(substituted) benzothiazolyl–N"–*n*–butyl guanidines are as follows :

Substituent –X–	Yield %	M.P. °C.		Elemental analysis, % Found	Calcd.
5-Chloro– ..	85	202	N,	14·98	15·03
			S,	8·44	8·59
4-Ethoxy– ..	80	79	N,	14·50	14·66
			S,	8·22	8·37

Pharmacological screening.—Pharmacological screening of these compounds has shown that N - *m* - tolyl - N' - 2 - (6 - chloro) benzothiazolyl-N"-methyl guanidine, N-*m*-tolyl-N'-2-(6-chloro) benzothiazolyl-N"-ethyl guanidine and N-*m*-tolyl-N'-2-(5-chloro) benzothiazolyl-N"-*n*-butyl guanidine are active at 100 μ g./ml. against *Myco. tuberculosis* ($H_{37}R$). The antibacterial activity of the compound No. 1-12 (Table III) has also been tested against *S. typhi, Staph. aureus* and—*comma* but the compounds were found to be inactive at 200 μ g./ml.

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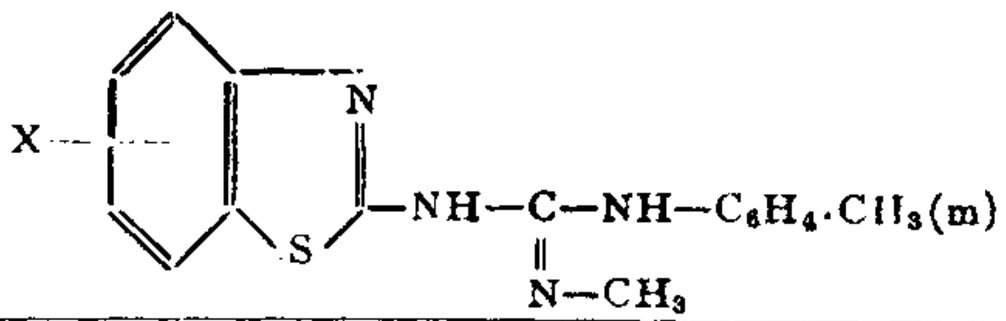
TABLE I

N-m-*tolyl*-*N'*-2-(*substituted*) *benzothiazolyl*-*N"*-*methyl guanidines*



Sl.No.	Nature of substituent -X-	Yield %	M.P. °C.	Molecular formula	Nitrogen, %		Sulphur, %	
					Found	Calcd.	Found	Calcd.
1	H	60	183	$C_{16}H_{16}N_4S$	18·81	18·92	10·77	10·81
2	4-Methyl-	83	112	$C_{17}H_{18}N_4S$	18·00	18·06	10·21	10·32
3	6-Methyl-	50	179	$C_{17}H_{18}N_4S$	18·10	18·06	10·30	10·32
4	4-Chloro-	70	151	$C_{16}H_{15}N_4SCl$	16·88	16·94	9·60	9·68
5	5-Chloro-	90	186	$C_{16}H_{15}N_4SCl$	16·90	16·94	9·69	9·68
6	6-Chloro-	60	111	$C_{16}H_{15}N_4SCl$	16·91	16·94	9·66	9·68
7	4-Methoxy-	65	165	$C_{17}H_{18}N_4SO$	17·01	17·18	9·79	9·81
8	4-Ethoxy-	85	107	$C_{18}H_{20}N_4SO$	16·36	16·47	9·37	9·41
9	6-Ethoxy-	80	136	$C_{18}H_{20}N_4SO$	16·44	16·47	9·40	9·41
10	6-Bromo-	75	135	$C_{16}H_{15}N_4SBr$	14·87	14·94	8·47	8·53

TABLE II

N-m-*tolyl*-*N'*-2-(*substituted*) *benzothiazolyl*-*N"*-*ethyl guanidines*

Sl. No.	Nature of substituent -X-	Yield %	M.P. °C.	Molecular formula	Nitrogen, %		Sulphur, %	
					Found	Calcd.	Found	Calcd.
1	H	80	98	$C_{17}H_{18}N_4S$	18·00	18·06	10·20	10·37
2	4-Methyl-	55	230	$C_{18}H_{20}N_4S$	17·13	17·28	9·77	9·88
3	5 Methyl-	50	161	$C_{18}H_{20}N_4S$	17·05	17·28	9·80	9·88
4	6-Methyl-	75	104	$C_{18}H_{20}N_4S$	17·14	17·28	9·81	9·88
5	4-Chloro-	45	196	$C_{17}H_{17}N_4SCl$	16·15	16·26	9·17	9·28
6	5-Chloro-	50	197	$C_{17}H_{17}N_4SCl$	16·20	16·26	9·21	9·28
7	6-Chloro-	70	90	$C_{17}H_{17}N_4SCl$	16·13	16·26	9·19	9·28
8	4-Methoxy-	75	132	$C_{18}H_{20}N_4SO$	16·36	16·47	9·30	9·41
9	4-Ethoxy-	65	110	$C_{19}H_{22}N_4SO$	15·77	15·82	9·00	9·04
10	6-Ethoxy-	60	106	$C_{19}H_{20}N_4SO$	15·73	15·82	9·01	9·04
11	6-Bromo-	45	215	$C_{17}H_{17}N_4SBr$	14·31	14·40	8·10	8·23

TABLE III

Antituberuclar activity of N-m-*tolyl*-*N'*-2-(*substituted*) *benzothiazolyl*-*N"*-*alkyl guanidines*

Sl. No.	-X-	Alkyl group	*Myco. tuberculosis* ($H_{37}R_v$) Activity in μg./ml.
1	6-Chloro-	Methyl.	Active at 100 μg./ml.
2	4-Chloro-	,,	Inactive at 200 μg./ml.
3	4-Methyl-	,,	,,
4	4-Methoxy-	,,	,,
5	6-Ethoxy-	,,	,,
6	6-Chloro-	Ethyl	Active at 100 μg./ml.
7	5-Chloro-	,,	Inactive at 200 μg./ml.
8	6-Methyl-	,,	,,
9	4-Ethoxy-	,,	,,
10	6-Ethoxy-	,,	,,
11	5-Chloro-	*n*-Butyl	Active at 100 μg./ml.
12	4-Ethoxy-	,,	Inactive at 200 μg./ml.

Streptomycin active at 1 ν/ml. against *Myco. tuberculosis* ($H_{37}R_v$)
Penicillin G. ,, 4 ν/ml. against *Staph. aureus*
Chloromycetin ,, 4 ν/ml. against *S. typhi*
I.N.H. ,, 0·4 ν/ml. against *Myco. tuberculosis* ($H_{37}R_v$)

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