to be significantly superior in meeting the disintegration test at all elevated storage conditions. PVdC blister packaging is found to be superior in protecting moisture pick up by the tablets. Moreover failure of all tablets stored at 45° and 75% RH to meet loss on drying test IP emphasizes the requirement of storage of pancreatin tablets in controlled humidity. In view of appreciable loss of enzyme activities on storage it is concluded that loss of enzyme activities should be taken into account in calculating percentage overage to be added for desired shelf life. Pancreatin tablets coated with acrycoat and blister packaged with PVdC (formula code AC-PVdC) was found to be better in all aspects compared to other formulations.

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Synthesis and Antimicrobial Activity of Some New Isoxazolines and 1,5-Benzothiazepines

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New six isoxazolines and five 1,5-benzothiazepines are synthesised from l-(substituted phenyl)-3-(2-methoxy-l-naphthyd-2-propen-l-ones. Their structural assignments are based on spectral data (IR and PMR) and elemental analysis. All these compounds have been screened for antimicrobial activity. The compounds with a methyl or chloro and methyl as well as chloro group on the aromatic ring showed good antimicrobial activity.

Nitrogen containing heterocyclic compounds like isoxazolines, nitrogen and sulphur containing heterocyclic compounds like benzothiazepines have received considerable attention in recent years due to their wide range of physiological activities. A number of isoxazole derivatives have been found to possess potential antibacterial[1] antitubercular[2], antifungal[3] and antidiabetic[4] activity. Anilidoisoxazolines synthesised by Zarif and Yammi[5] were found to possess remarkable bactericidal activity against some gram positive and gram negative bacteria. Mittal and Singhal[6] have reported antibacterial and antifungal activity in 3-methyl-4-(4'-bromo-2'-methyl benzene azo)-5-isoxazoline. Benzothiazepines such as diltiazen[7] or thiazesim[8] are constantly used as antidepressant, coronary vasodilator and antiangina agents. Levai[9] has reviewed the syntheses of four known groups of optically active 1,5-benzothiazepines. The references included show the most important biological activities like CNS, cardiotonic, histamine H_2 antagonistic and antiulcer. Bioassay screening of some substituted 1,5-benzothiazepines show mild analgesic and anticonvulsant activity[10]. These reports prompted us to synthesize new isoxazoline and benzothiazepine derivatives and evaluate their antimicrobial activity.

Melting points were determined in open capillaries and are uncorrected. The structures of the compounds were sup-

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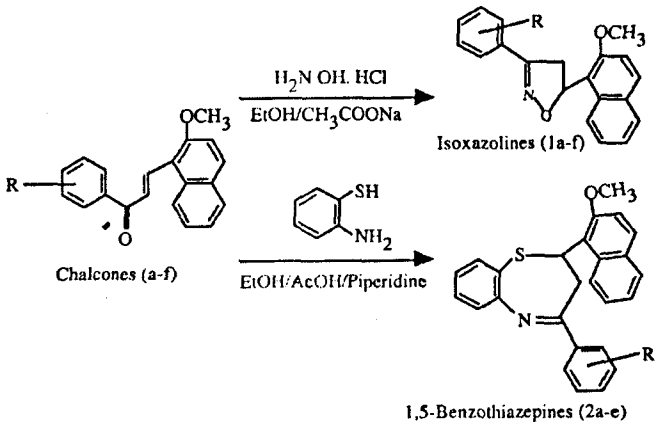
ported by elemental analysis and spectral data. The IR spectra (nujol) were recorded on a Beckman spectrophotometer (υ max in cm^{-1}) and PMR spectra obtained on a Gemini 200 spectrometer using $CDCl_3$ as solvent and TMS as an internal standard (δ in ppm). Elemental analysis (C,H,N and S) was carried out on a Carlo Ebra Strum DP 200.

1-(substituted phenyl)-3-(2-methoxy-1-naphthyl)-2-propen-1-ones, i.e., chalcones, on treatment with hydroxylamine hydrochloride in alcoholic sodium acetate under reflux yielded the respective isoxazolines[11] **1a-f** (yield 52-65%). Similarly some of the above chalcones were converted to the corresponding 1,5-benzothiazepines[12] **2a-e** (yield 66-72%) by treatment with o-aminothiophenol in alcoholic piperidine.



Scheme 1:

The compound If was synthesised by refluxing a mixture of 1-(3',5'-dichloro-2'-hydroxyphenyl)-3-(2-methoxy-1-naphthyl)-2-propen-1-one (3.73 g, 0.01 mol), and hydroxylamine hydrochloride (1.03 g, 0.015 mol) and sodium acetate (1.64 g, 0.02 mol) in ethanol (25 ml) for 5-6 h. The reaction mixture was cooled and poured into ice cold water. The solid product obtained was filtered, washed, dried and

TABLE 1: PHYSICAL DATA* AND ANTIMICROBIAL ACTIVITY OF ISOXAZOLINES (1a-f) AND 1, 5-BENZOTHIAZEPINES (2a-e).

Compd. No.	R	m.p. (°)	% yield	Antibacterial inhibition zone (mm)		Antifungal			
						C. lunata		*H. oryzae*	
				E. coli	*S. aureus*	germ-ination %	germ tube length (μ)	germ-ination %	germ tube length (μ)
1a	2'-OH	165	52	Nil	Nil	100	170	100	410
1b	2'-OH-5'-CH_3	198	52	42	28	100	210	100	144
1c	2'-OH-5'-C1	187	55	14	22	100	380	100	180
1d	2'-OH-5'-Br	188	55	10	22	100	240	90	400
1e	2'-OH-4'-CH_3-5'-C1	202	58	39.	24	100	310	95	305
1f	2'-OH-3',5'-di Cl	171	65	19	14	30	107	30	230
2a	2'-OH	214	70	Nil	14	100	185	100	480
2b	2'-OH, 5'-Cl	204	68	40	26	30	32	70	128
2c	2'-OH-5'-Br	194	66	21	17	100	165	100	280
2d	2'-OH-4'-CH_3-5'-C1	178	17	46	26	40	80	30	110
2e	2'-OH-3',5'-di Cl	216	72	42	24	30	60	60	80
Tetracycline				52	30	-	-	-	-
Water-ethanol (90:l0,v/v)				-	-	95.0	320	95.0	400

* All compounds gave satisfactory elemental analysis within ± 0.05% of theoretical values.

crystallised from ethanol yield : 3.09 g (65%); m.p: 171°.

Anal of If: IR (nujol) cm^{-1}:1605 (C = N); 1470, 1260 (N-O-C); 3370 (OH). PMR ($CDCl_3$) δ: 3.42-3.54 (dd, 2H, CH_2); 3.86 (s, 3H, OCH_3); 5.8-6.2 (t, 1H, CH); 7.0-8.2 (m, 8H, Ar-H); 10.82 (s, 1H, OH). The compounds 1a-f were prepared using a similar procedure as mentioned above.

The compound **2a** was synthesised by refluxing a mixture of 1-(2'-hydroxyphenyl)-3-methoxy-1-naphthyl)-2-propen-1-one (3.04 g, 0.01 mol) and o-aminothiophenol (1.25 g, 0.01 mol), few drops of piperidine in ethanol (50 ml) for 4 h. Thereafter glacial acetic acid (10 ml) was added to the reaction mixture and further refluxed for 2 h. The reaction mixture was left overnight at room temperature and the resultant solid obtained was filtered and crysyallised from ethanol-acetic acid yield: 3.0 g (70%); m.p: 214°. Anal of 2a: IR (nujol) cm^{-1}: 1610 (C=N); 3190 (OH). PMR ($CDCl_3$) δ: 3.73 (s, 3H, OCH_3) 3.24-3.32 (dd, 2H, CH_2); 6.31 (t, 1H, CH), 6.89-8.05 (m, 14H, Ar-H) and 14.6 (s, 1H, OH). Similarly other members of the series were prepared.

All the compounds have been screened for antibacterial activity against *Escherichia coli, Staphylococcus aureus* and antifungal activity against *Curvularia lunata, Helminthosporium oryzae* by the disc diffusion[13] and hanging drop[14] methods with slight modification. For antibacterial activity, the concentration of the compounds screened was 200 µg/ 0.1 ml. The zone of, inhibition of bacterial growth was measured after 24 h, after incubating at 37°. The results are tabulated in Table 1. The compounds with a methyl or chloro and methyl as well as chloro group (1b, 2c, 1e, 2b, 2d and 2e) on the aromatic ring showed potent antibacterial activity and all other compunds showed mild to moderate activity.

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