decreased level of physicial activity and sedentary life-style contributed in the progression of the disease. The impact of urbanization and its influence on life-style has been shown in an earlier study[14]. The present study suggested that educational interventional programme among these employees may be helpful.

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Synthesis and Antimicrobial Activity of Heterocyclic Schiff Bases, 4-Thiazolidinones and 2-Azetidinones

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Some new heterocyclic Schiff bases (1a-h), 4-thiazolidinones (2a-h) and 2-azetidinones (3a-h) have been synthesized and structures elucidated on the basis of elemental analysis, IR and ^{1}H NMR data. The antimicrobial screening data of the synthesized compounds are also presented.

Heterocyclic compounds of Schiff bases such as 4-thiazolidinones and 2-azetidinones are reported to be anticancer agents[1-3]. Schiff bases possess diversified biological applications[4-5]. Various 4-thiazolidinones show a variety of pharmacological activities[6-7]. Moreover compounds containing 2-azetidinone ring system are shown to possess marked biological activities[8-11]. Various 4-thiazolidinones inhibit the bacterial enzyme in biosynthesis of polymers[12]. All these observations and the essential role of heterocyclic compounds prompted us to synthesize Schiff

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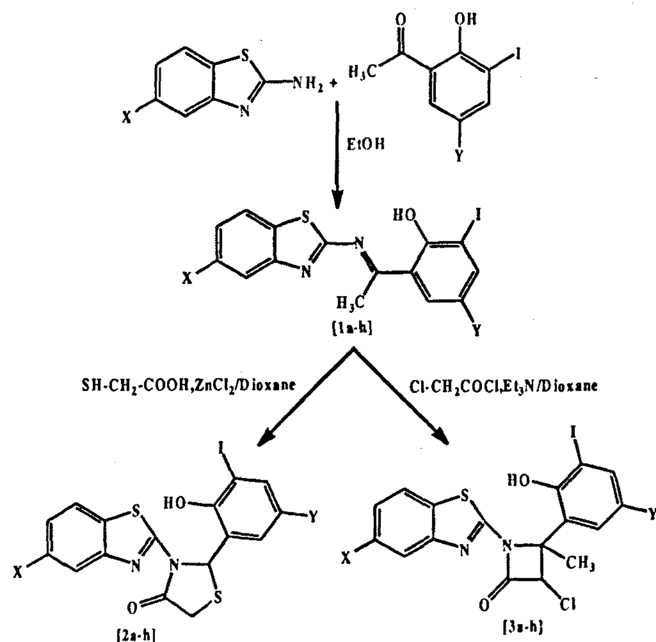
bases (1a-h), 4-thiazolidinones (2a-h) and 2-azetiditinones (3a-h).

2-Hydroxy-3-iodo-5-bromo/chloro acetophenones on condensation with 2-amino-6-substituted benzothiazole furnished the Schiff bases (1a-h). These Schiff bases on cyclo condensation with mercapto acetic acid in dioxane and in presence of anhydrous zinc chloride afforded 4-thiazolidinones (2a-h). Schiff bases (1a-h) on reaction with chloroacetyl chloride in dioxane and in presence of triethylamine yields 2-azetidinones (3a-h) (Scheme 1). Further the structure of compounds was deduced on the basis of spectral data (IR and ^{1}H NMR). Melting points were determined in open capillaries in a liquid paraffin bath and are uncorrected. Purity of compounds was checked by TLC. IR spectra were recorded in nujol on Perkin-Elmer-237 spectrophotometer. ^{1}H NMR were recorded in $CDCl_3$ on a Perkin-Elmer R-32 spectrometer using TMS as internal standard (Chemical shift are given in δ ppm).

To a mixture of 2-hydroxy-3-iodo-5-bromo acetophenone (10 mmol) and 2-amino-6-methoxy benzothiazole (10 mmol) dissolved in ethanol, one drop of acetic acid was added. The reaction mixture was refluxed for 2 h. The content were poured on ice cooled water, separated solid was dried and crystallized from ethanol to



Scheme 1: Synthetic scheme of Schiff bases, 4-thiazolidinones and 2-azetidinones.

give 2-N- (2-hydroxy-3-iodo-5-bromo-α-methyl benzylidene)-6-methoxy benzothiazole. IR (ν_{max}): 1630 (C=N) and 1590 (C=C). ^{1}H NMR ($CDCl_3$): 2.2 (s, 3H, CH_3), 4.2 (s, 3H, OCH_3), 6.9 -7.4 (m, 5H, Ar-H), and 7.5 (s, 1H, Ar-OH).

To a mixture of compound 1e (10 mmol) in dry dioxane (10 ml), mercapto acetic acid (10 mmol) in dry dioxane (10 ml) was added catalytic amount of zinc chloride and the reaction mixture was refluxed for 8 h. The reaction was monitored by TLC. Solvent was evaporated under reduced pressure and separated residue neutralized by sodium bicarbonate to remove excess of mercapto acetic acid. Solid compound obtained was crystallized from ethanol to give 2-methyl-2-(2'-hydroxy-3'-iodo-5'-bromophenyl)-3-(6''-methoxy benzothiazolyl)-4-thiazolidinone. IR (ν_{max}) 1659 (C=O) and 1586-1553 (C=C). ^{1}H NMR ($CDCl_3$): 2.4 (s, 3H, CH_3), 3.8 (s, 3H, OCH_3), 4.5 (s, 2H, CH_2S), 7.0-7.9 (m, 5H, Ar-H) and 8.9 (s, 1H, Ar-OH).

To a mixture of compound 1e (10 mmol) in dry dioxane (10ml), triethylamine (30 mmol), was added chloroacetyl chloride (12 mmol) drop wise at 10^0. The reaction mixture was stirred at room temperature for 6 h. The solvent was removed under reduced pressure, solid separated was dried and crystallized from chloroform to give 1-(6-methoxy benzothiazolyl)-3-chloro-4-methyl-4-(2'-hydroxy-3'-iodo-5'-bromophenyl)-2-azetidinone. IR (ν_{max}) 1741 (C=O) and 1646, 1519 (C=C). ^{1}H NMR ($CDCl_3$): 4.0 (s, 3H, OCH_3), 4.2 (s, 1H, CH-Cl), 4.6 (s, 3H, CH_3), 7.2-7.7 (m, 5H, Ar-H) and 9.2 (s, 1H, Ar-OH).

The compounds synthesized were screened for their antibacterial activity using *Escherichia coli*, *Salmonella typhi* and *Salmonella dysenterae* as bacteria. The activities of these compounds were tested using disc diffusion method[13] at 150 ppm concentration using 5 mm filter paper disc. Control experiment was carried out under similar condition by using tetracycline as a standard for comparison. The inhibition zone measured in mm showed that compounds 1a, 1d, 1h, 2a, 2g, 3a, and 3d were more active then other compounds tested against the above microbes, but none showed better or comparable activity to tetracycline.

The antifungal activity was tested[13] against the fungal species *Aspergillus niger*, *Penicillium notatum* and *Alternaria tenuissiama* at 150 ppm concentration. The antifungal data revealed the compounds 1d, 1e, 2d, 2h, 3b, and 3h were more active then other compounds tested against the above microbes, but none showed better or comparable activity to griseofulvin.

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TABLE 1: ANALYTICAL AND ACTIVITY DATA OF COMPOUNDS 1a-h, 2a-h AND 3a-h.

Entry	Molecular Formula	X	Y	M. P. (°)	Yield (%)	Bacteria[a]			Fungi[b]		
						Ec	St	Sd	An	Pn	At
1a	$C_{16}H_{12}N_2O_2SBrI$	OCH_3	Br	122	76	18	16	17	85	87	78
1b	$C_{16}H_{12}N_2OSBrI$	CH_3	Br	130	68	10	06	08	77	84	93
1c	$C_{15}H_9N_2OSBr_2I$	Br	Br	78	71	08	01	05	80	73	62
1d	$C_{15}H_9N_2OSBrClI$	Cl	Br	170	72	17	16	14	15	17	18
1e	$C_{16}H_{12}N_2O_2SClI$	OCH_3	Cl	65	70	07	04	06	17	15	19
1f	$C_{16}H_{12}N_2OSClI$	CH_3	Cl	79	68	04	05	07	84	86	68
1g	$C_{15}H_9N_2OSBrClI$	Br	Cl	111	75	05	04	03	51	87	72
1h	$C_{15}H_9N_2OSCl_2I$	Cl	Cl	89	73	18	17	15	74	65	56
2a	$C_{18}H_{14}N_2O_3S_2BrI$	OCH_3	Br	108	75	17	16	18	54	66	82
2b	$C_{18}H_{14}N_2O_2S_2BrI$	CH_3	Br	102	73	06	02	04	83	74	87
2c	$C_{17}H_{11}N_2O_2S_2BrI$	Br	Br	198	69	08	05	08	42	67	84
2d	$C_{17}H_{11}N_2O_2S_2ClBrI$	Cl	Br	262	65	04	05	07	18	15	17
2e	$C_{18}H_{14}N_2O_3S_2ClI$	OCH_3	Cl	90	70	10	05	08	88	77	64
2f	$C_{18}H_{14}N_2O_2S_2ClI$	CH_3	Cl	60	71	09	07	05	46	74	67
2g	$C_{17}H_{11}N_2O_2S_2BrClI$	Br	Cl	86	67	18	17	16	85	77	78
2h	$C_{17}H_{11}N_2O_2S_2Cl_2I$	Cl	Cl	68	65	08	04	07	18	17	16
3a	$C_{18}H_{13}N_2O_3SClBrI$	OCH_3	Br	78	70	15	17	18	94	67	51
3b	$C_{17}H_{11}N_2O_2SCl_2BrI$	CH_3	Br	108	69	07	05	04	18	15	17
3c	$C_{18}H_{10}N_2O_2SBrCl_2I$	Br	Br	135	66	04	03	01	58	77	54
3d	$C_{17}H_{10}N_2O_2SClBr_2I$	Cl	Br	65	63	19	17	18	45	67	63
3e	$C_{18}H_{13}N_2O_3SCl_2I$	OCH_3	Cl	52	71	05	04	03	54	47	45
3f	$C_{18}H_{13}N_2O_2SCl_2I$	CH_3	Cl	65	68	07	05	04	86	74	33
3g	$C_{17}H_{10}N_2O_2SCl_2BrI$	Br	Cl	97	65	08	04	06	58	67	73
3h	$C_{17}H_{10}N_2O_2SCl_3I$	Cl	Cl	72	64	10	08	04	18	17	15
Tetracycline						20	20	20	-	-	-
Greseofulvin						-	-	-	15	20	15

[a]Zone of inhibition in mm, [b]% of germination after 12 h. Ec stands for *Escherichia coli*, St for *Salmonella typhi* and Sd for *Salmonella dysenteriae*. An represents *Aspergillus niger*, Pn represents *Penicillium notatum* and At represents *Alternaria tenuissiama*.

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Simultaneous HPLC Estimation of Levonorgestrel and Ethinylestradiol from Tablets

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The present work describes a simple reverse phase HPLC method for the determination of levonorgestrel and ethinylestradiol from tablet formulations. The determination was carried out *on a Hypersil, ODS, C-18 (150x4.6 mm, 5 micron) column using a mobile phase of acetonitrile/* water (42:58). The flow rate and runtime were 2.2 ml/min and 7 min, respectively. The eluent was monitored at 210 nm. The method was found to be reproducible, with good resolution between levonorgestrel and ethinylestradiol. The detector response was found to be linear in the concentration range of 10-50 ppm for levonorgestrel and 2-10 ppm for ethinylestradiol.

Wide ranges of sterioďal hormones are used for contraception in a variety of formulations such as oral contraceptive pills (tablets), intra uterine devices and subcutaneous implants[1]. Literature survey indicated that HPLC, UV/Vis Spectrophotometer and potentiometry are used as official methods for the analysis of levonorgestrel and ethinylestradiol from tablets and pure drug[2-10]. The reported HPLC methods either lack the sensitivity or tedious, expensive and time consuming. The present investigation is an attempt to develop a highly sensitive, simple, precise and rapid analytical method for the simultaneous estimation of levonorgestrel and ethinylestradiol from tablet formulations.

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Standard samples of levonorgestrel and ethinylestradiol, which were prepared from reference standards procured from British Pharmacopoeia Commission, UK. HPLC grade acetonitrile manufactured by E. Merck was procured from commercial sources. Double distilled water was prepared in the laboratory. Oral contraceptive tablets containing levonorgestrel and ethinylestradiol were used obtained from local market and manufactured in in-house facility.

A Jasco HPLC system comprising a pump (Model: PU-980) with 20 μl loop, a UV/Vis detector (Model: UV-975) and integrator (Model: 807 IT) was used. The column used was