TABLE 2: RESULTS OF IN VITRO ANTIMICROBIAL ACTIVITY

| Compound No. | Zone of inhibition in mm* | | | | | |
|---------------|---------------------------|---------|------------|-------------|--|--|
| | Antibacterial | | Antifungal | | | |
| | S. aureus | E. coli | A. niger | C. albicans | | |
| 2 | 14 | 13 | 14 | 14 | | |
| 3 | 15 | . 15 | 13 | 15 | | |
| 4 | 13 | 14 | 18 | 14 | | |
| 5 | 15 | 15 | 16 | 17 | | |
| 6 | 16 | 13 | 16 | 17 | | |
| 7 | 09 | 13 | 22 | 16 | | |
| 8 | 14 | 16 | 22 | 25 | | |
| 9 | 15 | 15 | 13 | 15 | | |
| 10 | 15 | 10 | 13 | 18 | | |
| Ciprofloxacin | 20 | 21 | - | - | | |
| Griseofulvin | - | - | 26 | 25 | | |
| Control DMF | Nil | Nil | Nil | Nil | | |

^{*}Including diameter of the well - 8 mm.

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REFERENCES

- Weston, J.B., Eur. Pat. No., 1980, No. 7, 529, through Chem. Abstr., 1980, 93, 1502604u.
- Sengupta, A.K. and Avasthi, K., J. Indian Chem. Soc., 1975, 52, 847.
- 3. Sing, H. and Yadav, L.D.S., Agr. Biol. Chem., 1976, 40, 759.
- Vanderhock, R., Allen, G. and Settepani, J.A., J. Med. Chem., 1973, 16, 1305.
- 5. Basawaraj, R., Yadav, B. and Sangapure, S.S., Indian J. Heterocycl. Chem., 2001, 11, 31.

Antihypertensive Drug Utilization In Patients Attending Panjab University Health Centre

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The pilot study was carried out to assess prescribing practice of antihypertensive drugs at Panjab University Health Centre, Chandigarh. Prescriptions of hypertensive patients were monitored

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and data was filled as per WHO prescription Auditing Proforma. Study revealed that both monotherapy (48.5%) and combination therapy (51.5%) were employed to the patients. Among monotherapy calcium channel blockers (48.5%), β-blockers (45.5%) and angiotensin converting enzyme inhibitors (6.1%) were mainly prescribed. Among combination therapy, two-drug combination (39.7%) was most often prescribed. Highest prevalence of the disease was found among Class I employees that included administrative officers and teachers of the University. The study highlighted the current trend of antihypertensive drug prescribing in Panjab University Health Centre and pointed out the lacunae in the present prescribing practice.

Hypertension is the most important modifiable and treatable risk factor for cerebrovascular diseases, congestive heart failure, coronary artery disease and end-stage renal failure. The beneficial effect of antihypertensive drugs on cardiovascular outcome appears to be associated with the extent to which there is a lowering of diastolic and or systolic blood pressure and may be related to either reduction in progression of cardiovascular sequelae or reversing the endorgan damage^{1,2}. Various guidelines^{3,4} are available that recommended different classes of drugs to treat hypertension namely diuretics, β-blockers, calcium channels blockers, angiotensin converting enzyme (ACE) inhibitors and \(\beta\)-blockers. However, the selection of these as a firstline is still debatable and choice of antihypertensive drugs is influenced by factors such as the cardiovascular risk factor profile of the individual; presence of coexisting of disorders that may either favor or limit the use of a particular class of antihypertensive drugs.

Present study was conducted with an aim to establish the current prescribing pattern for antihyperstive drugs in Panjab University Health Centre (PUHC) and an attempt would be made to point out the lacunae in the present prescribing practice of Health Centre.

The PUHC, also named as Bhai Ghanayia ji caters to the health needs of the campus community consisting of students, faculty, non-teaching and administrative staff and their family members numbering about 25 000. Present pilot study was started just after getting approval from Institutional Ethical Committee of Panjab University as well as the official consent of chief medical officer (CMO). Data was collected on a semi structured coded performa which was framed as per WHO guideline⁵, from the patients attending the out patient department (OPD) through chance random sample method. At the initial stage doctors were not informed regarding the study protocol except CMO. This was done with an aim to establish the current trend of antihypertensive drug prescribing. During the study period (Dec to Feb), a total of 100 patients were monitored, of which 32 were excluded from the study because they either suffered from ischaemic heart dieseas such as angina, CHF,

TABLE 1: DEMOGRAPHIC DATA OF PATIENTS EMPLOYING MONOTHERAPY/ COMBINATION THERAPY

| | Male (N=37) | Female (N=31) | All Patients (N=68) |
|---------------------|-------------|---------------|---------------------|
| Age group (y) | | | |
| 40-49 | 8 (21.6%) | 6 (19.4%) | 14 (20.6%) |
| 50-59 | 17 (45.9%) | 14 (45.2%) | 31 (45.6%) |
| 60-69 | 10 (27.0%) | 6 (19.4%) | 16 (23.5%) |
| 70-79 | 2 (5.4%) | 4 (12.9%) | 16 (23.5%) |
| ≥80 | • | 1 (3.2%) | 1 (1.5%) |
| Mean age (y)±SD | 55.0±9.2 | 56.3±10.3 | 55.6±6.8 |
| Range (y) | 41-79 | 40-80 | 40-80 |
| Monotherapy | 22 (59.5%) | 11 (35.5%) | 33 (48.5%) |
| Combination therapy | 15 (40.5) | 20 (64.5%) | 35 (51.5%) |

N=number of patient, SD=standard deviation

TABLE 2: ANTIHYPERTENSIVE DRUG THERAPIES

| | Monotherapy (N=33) | Two-drug combination (N=27) | Three-drug combination (N=6) | Four-drug combination (N=2) |
|-------------------------|-----------------------|-----------------------------------|------------------------------------|-----------------------------------|
| Monotherapy vs. | | | | |
| combination therapy (%) | 48.5% | 39.7% | 8.8% | 2.9% |
| Combined therapy | - | 77.1% | 17.1% | 5.8% |

N=number of patients.

dysrrhythmias or diabetes or other co morbidities such as asthma and peptic ulcer diseases. Therefore, only 68 patients of any stage of hypertension were only included in the study. These patients were not new and had the history of hypertension for a long time and usually consult the physicians on fixed dates (first two weeks of each month) in each month as their prescription was refilled on monthly basis and also to reduce the rush during OPD timing.

Analysis of patient's data showed that hypertension was more prevalent in men (54.5%) as compared to women (45.6%). Mean age of the study population was 55.6 y (range 40-80 y), however majority of patients 79.4% (54 out 68) were above 50 y (Table 1). Consistent with the severities of hypertension, monotherapy was used more in men 59.5% (22 out of 37) while combination therapy was more prescribed in women 64.5% (20 out 31) as shown in Table 1. However, earlier studies have shown that, of the total hypertensive population only about 30% of patients can be adequately controlled with monotherapy while the remaining needed combination therapy⁶. This might be considered a favorable trend, provided blood pressure is adequately controlled to the targeted levels. Further these age group people were mostly Class I officers such as administrative officer or university teachers.

Monotherapy and combination therapy was used almost equally. Overall, 48.5% patients were treated with single antihypertensive drug and 51.5% were treated with antihypertensive drug combinations Table 2. Further among monotherapy three classes of drugs namely calcium channel blockers (CCBs) 48.5% (amlodipine in a dose range of 2.5-5.0 mg/day), β-blocker 45.5% (atenolol in a dose range 25-100 mg) and ACE inhibitor 6.1% (enalparil in dose range of 2.5-5.0 mg/d) were used. Overall utilization pattern was also similar with CCBs (amlodipine 66.2% and nifedipine SR 2.9%) being the most frequently prescribed class (69.1%), β-blockers (atenolol 66.2%) were marginally behind (66.2%), followed by ACE inhibitors 12.0% (enalapril 9% and

ramipril 2.9%) and diuretics 10.3% (triamtrene and benzthiazide combination ditide 7.4%, chlorthalidone 1.5% and indapamide 1.5%) utilization of two, three and four drugs was 77.1%, 17.1% and 5.8%, respectively. However, diuretics is one class of antihypertensives that are most extensively studied and recommended as first-line therapy for treatment of hypertension. The overall utilization of diuretics was much lower in the present study (10.3%) as compared to earlier study at Bahrain7. This might be due possible adverse effects of diuretics on glucose homeostasis and lipid profile8 and sexual function9 in male may account for the reluctance of physicians to prescribe this class of antihypertensive. The prescribing of ACE inhibitors was found to be much lesser in the present study. In combination therapy, 39.7%, 8.8% and 2.9 % were prescribed as two drug combinations, three and four drug combinations respectively Table 2. In total combination therapies, twodrug combination was mostly prescribed (77.1%) of atenolol and amlodipine combination was most frequently prescribed 81.5 % of cases (22 out 27). Administration of a β -blocker with a dihydropyridine (DHP) class of CCB constitutes very effective and generally well-tolerated two antihypertensive combination therapies 10. In this form of combination and in addition to its favorable complementary synergistic effects, a β-blocker tend to blunt the troublesome complementary reflex tachycardia induced by short-acting DHP class of CCBs and the latter may, additionally counteract any peripheral vasoconstriction caused by the former. Their combined efficacy has been confirmed 10,11 without causing adverse drug interaction or poor tolerability. Such combinations were ranked as first and second most frequently prescribed therapy in surveys conducted in Hong Kong¹² and in Finland¹³ respectively. In our study population, 40 (58.8%) were grade I employees (university teachers and administrative officers), 24 (35.3) were grade II (clerical staff) and 4 (5.9%) were grade III employees (gardeners, security guards and peons). Greater prevalence of the disease among grade I employee might be due to their

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 study¹⁴. The present study suggested that educational interventional programme among these employees may be helpful.

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REFERENCES

- 1. Hansson, L., J. Hypertension, 1996, 14, 527.
- Hansson, L. and Dahlof, B., In; Largh, J.H. and Brener, B.M. Eds., Hypertension: Pathophysiology, Diagnosis and Management, Raven Press, New York, 1990, 2131.
- 3. Zanchetti, A., J. Hypertension, 1995, 13, 119.
- The Sixth Report of the joint national committee on prevention, Detection, Evaluation and Treatment of high blood pressure, Arch. Intern. Med, 1997, 157, 2413.

- Bimo, Chowdhary, A., Das, A., Diwan, V., Kafle, K.K., Mabadeje, B., Massele, A., Laing, R.O., Ofori-Adjei, D., Ross-Deganan, D., Santoso, B. and Tomson, G., In; How to investigate drug use in health facilities (selected drug use indicator) action programme on essential drugs, WHO official publication, 1995, 68.
- Hansson, L., Zanchetti, A., Carruthers, S.G., Dahlof, B., Elmfeldt, D., Julius, S., Menard, J., Rahn, K.H., Wedel, H. and Westerling, S., Lancet, 1998, 251, 1755.
- Khaja, K.A.J.A., Sequeira, R.P., Wahab, A.W.M.A. and Mathur, V.S., Pharmacoepidemiol. Drug Saf., 2001, 10, 219.
- Osei, K., Holland, G. and Falko, J.M., Arch. Intern. Med., 1986, 146, 1973.
- 9. Brock, G.B. and Lue, T.F., Drug Safety, 1993, 8, 414.
- Hansson, L., Dahlof, B., Gudbrandsson, T., Hellsing, T., Kullman, S., Kuylenstierna, J., Leppert, J., Moller, B., Skogstrom, K. and Svensson, A., J. Cardiovasc. Pharamacol., 1988, 12, 94.
- Dahlof, B and Hosie, J., J Cardiovasc. Pharmacol., 1990, 16, 910.
- Lee, P.K., Li, R.K., Chan, J.C., Chang, S., Lee, S.C., Tomlinson, B. and Critchley, J.A., Brit. J. Clin. Pharmacol., 1997, 44, 577.
- Wallenius, S., Kumpusalo, E., Parnanen, H. and Takala, J., Eur, J. Clin. Pharmacol., 1998, 54, 793.
- 14. Ramachandran, A., Snehalatha, C., Latha, E., Manoharan, M. and Vijay, V, Diabetes Res. Clin. Pract., 1999, 44, 207.

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 ¹H 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

*For correspondence E-mail: bhusare71@yahoo.com Department of Medicinal Chemistry, School of Pharmacy, The Hebrew University of Jerusalem, Jerusalem-91120, Israel. anticancer agents¹⁻³. Schiff bases possess diversified biological applications⁴⁻⁵. Various 4-thiazolidinones show a variety of pharmacological activities⁶⁻⁷. Moreover compounds containing 2-azetidinone ring system are shown to possess marked biological activities⁸⁻¹¹. Various 4-thiazolidinones inhibit the bacterial enzyme in biosynthesis of polymers¹². All these observations and the essential role of heterocyclic compounds prompted us to synthesize Schiff