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α-GLUCOSIDASE AND CHYMOTRYPSIN INHIBITING LIGNANS FROM *COMMIPHORA MUKUL*

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Abstract: Phytochemical investigation of the whole plant of *Commiphora mukul* Engl. resulted in the isolation of two lignans, epiexcelsin (**1**) and 5′-demethoxyepiexcelsin (**2**) which are reported for the first time from this species. The structure elucidation of the isolated compounds was based on 1D and 2D-NMR analysis and by the comparison with the published data. The lignans **1** and **2** showed significant inhibitory activity against α-glucosidase with the IC_{50} of 59.8 ± 3.63455 μM and 75.2 ± 8.1616 μM respectively. They also showed weak inhibitory potential against chymotrypsin with the IC_{50} of 110 ± 0.025 μM and 649 ± 0.013 μM respectively.

Keywords: *Commiphora mukul*, ligans, α-glucosidase, chymotrypsin, inhibitors

Introduction

Commiphora mukul Engl. (Guggul) is a medicinal plant, which has a wide range of usefulness in indigenous medicine. Like all oleo-resins, it causes an increase of leucocytes in the blood and stimulates phagocytosis [1]. Guggulu is the gum-resin exudate from the tree *Commiphora mukul* and is efficacious in the treatment of rheumatoid arthritis, obesity and allied disorders besides several other therapeutic uses. Pharmacological studies on the crude drug as well as on some of its fractions and pure constituents have revealed significant anti-inflammatory, anti-rheumatic and hypocholestremic/hypolipaemic activity [2]. Enzyme inhibition is an important area of pharmaceutical research since studies in this field have already led to the discovery of wide variety of drugs useful in a number of diseases. Specific inhibitors interact with enzymes and block their activity towards their corresponding natural substrates. The importance of enzyme inhibitors as drugs is enormous since these molecules have been used for treating a number of physiological conditions [3]. The lignans **1** and **2** showed inhibitory activity against α- glucosidase and chymotrypsin enzymes.

α- Glucosidase catalyzes the final step in the digestive process of carbohydrates. Its inhibitors can retard the uptake dietary carbohydrates and suppress postprandial hyperglycemia, and could be useful to treat diabetic and /or obese patients [4]. α- Glucosidase inhibitors are effective in lowering the insulin release, insulin requirement and some lower plasma lipids. They have been suggested as inhibitors of tumor metastasis, antiobesity drugs, fungistatic compounds, insect antifeedents, antivirals and immune modulators [5]. Inhibition of α-glucosidase causes abnormal functionality of glycoproteins because of incomplete modification of glycans. Suppression of this processing is to be expected for antiviral activity and decreasing of growth rate of tumors [6]. Serine proteases such as chymotrypsin and trypsin are involved in the destruction of certain fibrous proteins [7]. Chronic infection by hepatitis

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C virus can lead to the progressive liver injury, cirrhosis, and liver cancer. A chymotrypsin like serine protease known NS3 protease is taught to be essential for viral replication, has become target for anti-HCV drugs [8].

Materials and Methods

General

For column chromatography (CC), silica gel (70-230 mesh) and for flash chromatography (FC), silica gel (230-400 mesh) was used. TLC was performed on pre-coated silica gel G-25-UV_{254} plates. Detection was carried out at 254 nm, and by ceric sulphate reagent. Purity was checked on TLC with different solvent systems using hexane, acetone and $CHCl_3$ giving single spot. The optical rotations were measured on a Jasco-DIP-360 digital polarimeter. The UV and IR spectra were recorded on Hitachi-UV-3200 and Jasco-320-A spectrophotometer, respectively. ^{1}H-NMR, ^{13}C-NMR, COSY, HMQC and HMBC Spectra were run on Bruker spectrometers operating at 500, 400 and 300 MHz. The chemical shifts are given in δ in ppm and coupling constants in Hz. EI-MS spectra were recorded on a JMS-HX-110 spectrometer, with a data system.

Plant material

Commiphora mukul Engl. was purchased from Liaquatabad supermarket, Karachi and identified by Dr. Surayya Khatoon, Department of Botany, University of Karachi. The voucher specimen of the plant is deposited in the herbarium of the Botany Department of the same University.

Extraction and purification

The shade-dried ground whole plant (20 Kg) was exhaustively extracted with methanol at room temperature. The extract was evaporated to yield the residue (285 g). The whole residue was extracted with hexane, chloroform, ethyl acetate and butanol. The chloroform soluble fraction (135 g) was subjected to CC over a silica gel column using hexane with gradient of acetone up to 100 % and followed by methanol. Eight fractions (Fr. 1-8) were collected. The Fr. 4 was loaded on silica gel (flash silica 230-400 mesh) and eluted with acetone: hexane (1.5: 8.5) to purify **2** and **1** respectively.

Epiexcelsin (**1**). White Powder (26.9 mg): $C_{22}H_{22}O_8$; $[\alpha]^{23}_D$ + 88° (*c* = 0.14, $CHCl_3$); UV λ_{max} nm (logε) (MeOH): 389 (1.21), 280 (1.57), 265 (1.82), 213 (3.03), 199 (4.12) nm; IR ν_{max} ($CHCl_3$): 2959 (C-H Ar), 1365,1137 (C-O-C), 812, 756 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 6.56 (1H, d, *J* = 1.5 *Hz*, H-6″), 6.54 (1H, d, *J* = 1.4 *Hz*, H-6′), 6.51 (1H, d, *J* = 1.4 *Hz*, H-2′), 6.48 (1H, d, *J* = 1.5 *Hz*, H-2″), 5.94 (2H, s, H-7″), 5.93 (2H, s, H-7′), 4.78 (1H, d, *J* = 5.4 *Hz*, H-6), 4.34 (1H, d, *J* = 7.1 *Hz*, H-2), 4.07 (1H, m, H_b-4), 3.89 (6H, s, H-8″ & H-8′), 3.79 (2H, m, H_b-8, H_a-4), 3.28 (1H, m, H_a-8), 3.25 (1H, m, H-5), 2.82 (1H, m, H-1); ^{13}C-NMR (100 MHz, $CDCl_3$): 149.0 (C-3′), 148.9 (C-3″), 143.6 (C-5′), 143.5 (C-5″), 135.9 (C-1′), 134.7 (C-4′), 134.2 (C-4″), 132.9 (C-1″), 105.7 (C-6″), 105.2 (C-6′), 101.4 (C-7″), 101.3 (C-7′), 100.1 (C-2′), 99.9 (C-2″), 87.6 (C-2), 82.0 (C-6), 70.9 (C-4), 69.6 (C-8), 56.6 (C-8′ & C-8″), 54.5 (C-1), 50.0 (C-5); EIMS *m/z* (rel. int.): 414 $[M]^+$ (79), 234 (15), 233 (20), 208 $[ArCH:CHCH2OH]^{\cdot+}$ (37), 203 (17), 191 $[ArCH:CHCH_2]^+$ (53), 181 $[ArCHOH]^{\cdot+}$ (50), 180 $[ArCOH]^{\cdot+}$ (68), 179 $[ArCO]^{\cdot+}$ (100), 165 $[ArCH_2]^+$ (94), 161 (26), 153 $[ArH_2]^+$ (44), 152 $[ArH]^+$ (44), 151 $[Ar]^+$ (31).

5′-Demethoxyepiexcelsin (**2**). Gummy solid (15.4 mg): $C_{21}H_{20}O_7$; $[\alpha]^{23}_D$ + 116.3 (*c* = 1.35, $CDCl_3$); UV λ_{max} nm (log ε) (MeOH): 278 (1.94),

262 (1.51) 210 (4.27), 198 (2.83), 196 (4.90) nm; IR ν_{max} ($CHCl_3$): 2964 (C-H, Ar), 2863 (C-H, Aliphat), 1634, 1450 (C=C, Ar), 1322, 1080 (C-O-C), 832, 736, 670 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 6.84 (1H, d, *J* = 1.6 *Hz*, H-2′), 6.78 (1H, dd, *J* = 1.6 *Hz*, H-6′), 6.74 (1H, d, *J* = 7.8 *Hz*, H-5′), 6.56 (1H, d, *J* = 1.5 *Hz*, H-6″), 6.48 (1H, d, *J* = 1.5 *Hz*, H-2″), 5.95 (2H, s, H-7″), 5.92 (2H, s, H-7′), 4.78 (1H, d, *J* = 5.4 *Hz*, H-6), 4.36 (1H, d, *J* = 7.1 *Hz*, H-2), 4.06 (1H, m, H_b-4), 3.89 (3H, s, H-8″), 3.81 (2H, m, H_b-8, H_a-4), 3.29 (1H, m, H_a-8), 3.25 (1H, m, H-5), 2.82 (1H, m, H-1); ^{13}C-NMR (100 MHz, $CDCl_3$): 148.8 (C-3″), 147.9 (C-4′), 147.2 (C-3′), 143.5 (C-5″), 135.0 (C-1′), 134.1 (C-4″), 132.9 (C-1″), 119.5 (C-6′), 108.1 (C-5′), 106.5 (C-2′), 104.8 (C-6″), 101.4 (C-7″), 101.0 (C-7′), 99.8 (C-2″), 87.6 (C-2), 82.0 (C-6), 70.9 (C-4), 69.6 (C-8), 56.6 (C-8″), 54.5 (C-1), 50.1 (C-5); EIMS *m/z* (rel. int.): 384 $[M]^+$ (46.9), *m/z* 208 $[ArCH{:}CHCH_2OH]^{+}$ (11.6), 179 [Ar″ $CH{:}CHCH_2OH$] (36.1), 151 [Ar^+] (16.8), 149 [Ar″ CO^+] (100), 135 [Ar″ CH_2^+] (70.9) and 122 [Ar″ H^+] (12.9).

In vitro α-glucosidase inhibition assay

The inhibitory activity of the compounds **1** and **2** has been determined against α-glucosidase, (E.C. 3. 2. 1. 20), type VI from Brewers yeast purchased from Sigma (G-6136). The inhibition has been measured spectrophotometrically at pH. 6.8 and at 37 °C using 0.7 mM *p*- nitrophenyl α-D glucopyranoside (PNP-G) as a substrate and 0.017 units/ ml enzyme, in 50 mM sodium phosphate buffer containing 100 mM NaCl. 1 –Deoxynojirimycin (0.3 mM) was used as a positive control [9]. The increment in absorption at 400 nm due to the hydrolysis of PNP-G by α-glucosidase was monitored continuously with the spectrophotometer (Molecular Devices USA) [10].

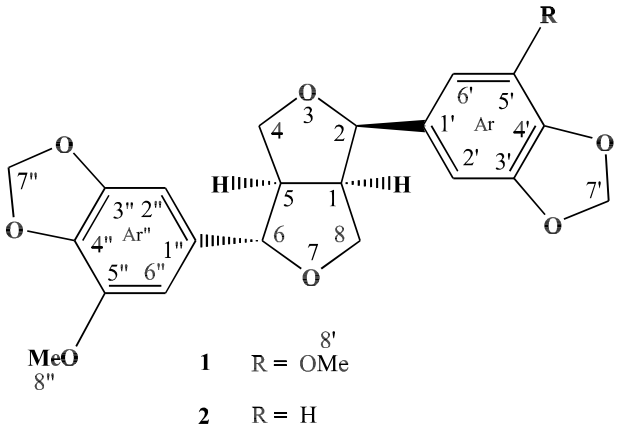

Figure 1. Structure of compounds 1 and 2.

In vitro chymotrypsin inhibition assay

The α-chymotrypsin inhibitory activity was performed by the reported method [11]. Chymotrypsin (9 units/ ml of 50 mM Tris-HCl buffer pH 7.6; Sigma Chemical Co. USA) was preincubated with the compounds for 20 min at 25 °C. 100 µl of substrate solution (N-succinyl-phenylalanine-*p*-nitroanilide, 1mg/ ml of 50 mM Tris-HCl buffer pH 7.6) were added to start the enzyme reaction. The absorbance of released *p*-nitroaniline was continuosly monitored at 410 nm until a significant color change had achieved. The final DMSO concentration in the reaction mixture was 7 %.

Results and Discussion

From the chloroform soluble fraction of *Commiphora mukul* Engl. two lignans, epiexcelsin (**1**) [12] and 5′-demethoxyepiexcelsin (**2**) [13] were isolated for the first time from this species. The NMR data (see experimental part) of these compounds indicated to be 2,6-diaryl-3, 7-dioxabicylo [3,3,0]-octanes, i.e. lignans of the fused bistetrahydrofuran series [12]. In lignans of this class three types of stereoisomers are possible, the isomer with both aryl groups axial, the isomer with both aryl groups

equatorial and the third isomer with one aryl group axial and one equatorial [12]. These lignans belonged to third type of stereoisomers and displayed significant inhibitory activity against α-glucosidase and weak against chymotrypsin. Their IC_{50} values are shown in the table 1. 1-Deoxynojirimycin and chymostain were used as positive controls for α-glucosidase and chymotrypsin enzymes, respectively.

Table 1. *In vitro* quantitative inhibition of α-glucosidase and chymotrypsin by epiexcelsin (**21**) and 5´-demethoxyepiexcelsin (**22**).

Name of the Substance	IC_{50} ± SEM[a] [μM] α-Glucosidase	Chymotrypsin
Epiexcelsin (**21**)	59.8 ± 3.63455	110 ± 0.025
5´-Demethoxyepiexcelsin (**22**)	75.2 ± 8.1616	649 ± 0.013
Positive control	1-Deoxynojirimycin)[b] 410 ± 8.055	Chymostain)[c] 8.23 ± 0.0024

[a] Standard mean error of five assays.

[b] positive control for α-glucosidase; [c] for chymotrypsin.

From the IC_{50} values of both these lignans, it is clear that they have significant inhibitory potential as compared to that of 1-deoxynojirimycin, which was used as a positive control for α-glucosidase enzyme, but they are weak inhibitor relative to the positive control (chymostain) of chymotrypsin enzyme. However, in terms of structure-activity relationship, the more inhibitory potential of epiexcelsin (**21**) against α-glucosidase and chymotrypsin, as compared to that of 5´-demethoxyepiexcelsin (**22**), can be attributed to the presence of similar aryl groups on the both sides of 3, 7-dioxabicyclo [3,3,0]-octane unit. In other words, the absence of a methoxyl group on C-5´ of 5´-demethoxy-epiexcelsin (**22**), resulted in a decrease of inhibitory activity against α-glucosidase and chymotrypsin as compared to that of epiexcelsin (**21**).

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REGULARIZATION OF A SYSTEM OF THE THIRD-KIND VOLTERRA EQUATIONS

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Abstract: In this paper the regularization problem of a System of Volterra Integral Equations of the third kind is investigated. The space of continuous functions that contain operator multiplied by non-increasing function is considered. In this paper Michael M. Lavrentiev Regularization Method is applied to linear and nonlinear equations. The set of regularization system and sufficient conditions of uniqueness of solution were obtained. It is proved that in certain conditions the scheme of regularization keeps all the properties of Volterra type equations, and gives a uniform approximation to an exact solution of the original problem.

***Keywords*:** Ill posed problems, inverse problem, perturbations theory, approximate solution, uniqueness of the solution, coefficient of continuity.

Introduction

To solve a problem of fluid transfer, which depends on degree of a non-stationarity of drying process and of the non-homogeneity of the media, one has to solve a generalized problem of standard diffuse model of fluids transfer. The law of Henry Darcy (1856) governs the flow of groundwater through granular media or the flow of other fluids through permeable material, such as petroleum through sandstone or limestone and modeled by the partial equation of the third order [1], which is nonlinear in general case. In the linear case inverse non-local boundary problem of determining the coefficients of the third order differential equation are reduced to the Volterra integral equations of the third kind. One of the most effective methods of solving these integral equations is the Regularization Method. General basics of regularization of Volterra integral equations of the first kind are given in [2-4]. The survey of Regularization Method is given in [5]. Regularization by Tihonov [2] of the Volterra integral equations of the first kind supposes transfer to the self-conjugate operator and loses the property of Volterra operator, and therefore is not applicable for a space of continuous functions. M. Lavrentiev discovered the method of regularization of Volterra integral equation of the first kind [3]. The main idea of Lavrentiev's Method consists of following: an equation $Au = f$ is an ill-posed problem in general, where A is a continuous operator. This equation is substituted by the equation $\varepsilon u + Au = f$, where ε is a small parameter. A solution of latter is called regularized solution of original equation. Regularized solution is an approximation to the exact solution of original problem.

The regularization of the Volterra integral equation of the third kind with non-decreasing function discovered by M. Imanaliev and A. Asanov in [4]. In [6] the regularization of this

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problem was investigated for special condition on kernel of integral operator.

In this paper we employ Lavrentiev regularization method for a linear and non-linear system Volterra integral equation of the third kind with non-increasing function. The regularization of these systems is considered in the space of continuous function. Using inversion of regularized equation we obtain Volterra integral equation of the second kind. The existence and uniqueness of a solution of this equation is provided by introduced conditions. This technique is unrealizable for original equation because the kernel of equation may vanish on the diagonal.

The distinguishing result of this set of methods is that the property of Volterra operator is not lost.

Regularization of a Linear System

Let us consider the system of linear integral equations in the space of continuous functions $C_n[0,b]$,

$$p(x)\upsilon(x)+\int_0^x K(x,t)\upsilon(t)dt = f(x). \qquad (1)$$

Let known scalar function $p(x)$, vector - function $f(x)$ and matrix - function $K(t,x)$ satisfy the following condition:

a) $f(x)\in C_n^1[0,b]$, $p(x)\in C[0,b]$, $p(b)=0$, $p(x)$ – non increasing function;

b) $K_{i,j}(x,t)\in C(D)\cap Lip(x|L_K)$, $i,j=1,2,\ldots,n$, $\lambda_1(x),\ldots,\lambda_n(x)$ - eigenvalues of the matrix $[K(x,x)+K^*(x,x)]/2$,

where $K^*(x,x)$ - matrix, conjugated to $K(x,x)$, and, $0\le\lambda_0(x)=\min\{\lambda_i(x)|1\le i\le n\}$, $0<L_K=const$, $D=\{0\le t\le x\le b\}$.

Lemma 1. (1) is equivalent to the following system of integral equations

$$(A\upsilon)(x)+(G\upsilon)(x)=(L\upsilon)(x)+g(x), \qquad (2)$$

where $(A\upsilon)(x)=p(x)\upsilon(x)$,

$$(G\upsilon)(x)=\int_0^x G(t)\upsilon(t)dt,$$

$$G(x)=C_0p(x)+K(x,x),\ 0<C_0=const,$$

$$(L\upsilon)(x)=\int_0^x L(x,t)\upsilon(t)dt,$$

$$L(\tau,t)=K(t,t)-K(x,t)-C_0\int_t^x K(v,t)dv,$$

$$g(x)=f(x)+(Jf)(x),\ (Jf)(x)=C_0\int_0^x f(t)dt,$$

Proof. Suppose (1) has a solution. Substituting this solution into (2) yields, that any arbitrary solution of (1) also is the solution of (2), because

$$(A\upsilon)(x)+(K\upsilon)(x)-f(x)=-J[(A\upsilon)(x)+(K\upsilon)(x)-f(x)].$$

Now let $\upsilon(x)$ be a solution of (2). Let us suppose that this function is not satisfying (1). Substituting $\upsilon(x)$ into (1) we get

$$(A\upsilon)(x)+(K\upsilon)(x)-f(x)=\tilde{R}(x).$$

But from (2) we also get homogeneous integral equation of second kind

$$\tilde{R}=J\tilde{R},$$

from which follows that $\tilde{R}(x)\equiv 0$. QED

According to Lavrentiev method, the corresponding system of equations with a small parameter ε « 1 has a form

$$(\varepsilon I+A)\upsilon_\varepsilon(x)+(G\upsilon_\varepsilon)(x)=(L\upsilon_\varepsilon)(x)+\varepsilon\upsilon(0)+g(x) \qquad (3)$$

where I is a unit operator.

Let there exist positive numbers θ_1, θ_2 and C_0, such that following conditions are satisfied

$$0 < d_1 \le C_0 p(x) + \lambda_0(x),$$
$$\theta_1(C_0 p(x) + \lambda_0(x)) + p'(x) \ge 0,\ \theta_1 + \theta_2 = 1. \quad (4)$$

Let us introduce an operator H_ε

$$(H_\varepsilon \upsilon)(x) = -\frac{1}{\varepsilon + p(x)} \int_0^x W_\varepsilon(x,t) G(t) \frac{\upsilon(t) - \upsilon(x)}{\varepsilon + p(t)} dt$$
$$+ \frac{W_\varepsilon(x,0)}{\varepsilon + p(x)} (\upsilon(x) - \upsilon(0)) \quad (5)$$

where $W_\varepsilon(x,t) = \exp(-\int_t^x \frac{G(s)}{\varepsilon + p(s)} ds)$ - matrix function, satisfying Vajevski inequality [6]

$$\|W_\varepsilon(x,t)\| \le \exp(-\int_t^x \frac{\lambda(s)}{\varepsilon + p(s)} ds)\sqrt{n},$$
$$\lambda(x) = C_0 p(x) + \lambda_0(x). \quad (6)$$

Lemma 2. Let the conditions *a)-b)*, (4), $\|G(x)\| \le C_1 \lambda(x)$, $0 < C_1 = const$ and $\upsilon(x) \in C_n^\gamma[0,b]$, $0 < \gamma \le 1$ are satisfied. Then there is an estimate

$$\|\varepsilon(H_\varepsilon \upsilon)(x)\|_{C_n} \le$$
$$d_0 (C_1 \theta_2^{-(1+\gamma)} d_2 d_1^{-\gamma} + p_0^{-1} \varepsilon^{1-\gamma} b^\gamma) \sqrt{n} \varepsilon^\gamma, \quad (7)$$

where $d_0 = \sup_{(x,s)\in[0,b]} \{\frac{\|\upsilon(x) - \upsilon(s)\|}{|x-s|^\gamma}\}$,

$$d_2 = \int_0^\infty \sigma^\gamma e^{-\sigma} d\sigma,\ p_0 = p(0).$$

Proof. For the second term of (5) using equality

$$\exp(-\int_t^x \frac{p'(s)ds}{\varepsilon + p(s)}) = \frac{\varepsilon + p(t)}{\varepsilon + p(x)} \quad (8)$$

we obtain the estimation

$$\frac{1}{\varepsilon + p(x)} \exp(-\int_0^t \frac{G(s)ds}{\varepsilon + p(s)}) \|\upsilon(x) - \upsilon(0)\| \le$$
$$\frac{\sqrt{n}}{\varepsilon + p(0)} d_0 b^\gamma.$$

Multiplying the first term of (5) by ε and using (4), we obtain

$$\|\frac{\varepsilon}{\varepsilon + p(x)} \int_0^x W_\varepsilon(x,t) G(t) \frac{u(x) - u(t)}{\varepsilon + p(t)} dt\| \le$$
$$\int_0^x \exp(-\theta_2 \int_t^x \frac{\lambda(s)}{\varepsilon + p(s)} ds) \times$$
$$\times \left(\int_t^x \frac{\lambda(s)}{\varepsilon + p(s)} ds \right)^\gamma C_1 \sqrt{n} d_0 d_1^{-\gamma} \frac{\varepsilon}{[\varepsilon + p(t)]^{1-\gamma}} \frac{\lambda(t)}{\varepsilon + p(t)} dt \le$$
$$d_0 C_1 \theta_2^{-(1)\gamma}\ d_2 d_1^{-\gamma} \sqrt{n} \varepsilon^\gamma$$

which was to be the proof. QED

Theorem 1. Let conditions *a)-b)*, the estimations (4) and $\|G(x)\| \le C_1 \lambda(x)$ take place, and the solution of the equation (1) is $\upsilon(x) \in C_n^\gamma[0,b]$, $0 < \gamma \le 1$. Then the solution of (3) uniformly converges to the solution of (1) with $\varepsilon \to 0$, and there is an estimate

$$\|\upsilon_\varepsilon(x) - \upsilon(x)\|_{C_n} \le d_3 \varepsilon^\gamma, \quad (9)$$
$$d_3 = d_0 (C_1 \theta_2^{-(1+\gamma)} d_2 d_1^{-\gamma} + p_0^{-1} \varepsilon^{1-\gamma} b^\gamma) \exp(b C_3 (L_K + C_0 K_1)/d_1),$$
$$K_1 = \max_D \|K(x,t)\|,$$
$$C_3 = (2 C_1 \theta_2^{-2} + \|\varphi(x)\|_C / p(0)) \sqrt{n},$$
$$\varphi(x) = \int_0^x \lambda(t) dt.$$

Proof. Let us make substitution in (3)

$$\upsilon_\varepsilon(x) = \upsilon(x) + \eta_\varepsilon(x). \quad (10)$$

Then we obtain the following system of equations with respect to $\eta_\varepsilon(x)$

$$(\varepsilon I + A)\eta_\varepsilon(x) + (G\eta_\varepsilon)(x) = (L\eta_\varepsilon)(x) - \varepsilon[\upsilon(x) - \upsilon(0)].$$

Apparently, taking into account (5), inverse of this system can be found

$$\eta_\varepsilon(x) = (H_\varepsilon[L\eta_\varepsilon])(x) - \varepsilon(H_\varepsilon\upsilon)(x). \qquad (11)$$

For matrix function $L(x,t)$ the following estimation is fulfilled

$$\|L(x,v) - L(s,v)\| \le d_1^{-1}(L_K + C_0K_1)[\varphi(x) - \varphi(s)].$$

and

$$\|(H_\varepsilon[L\eta_\varepsilon])(x)\| \le [C_1 \frac{2\sqrt{n}}{\varepsilon + p(x)}$$

$$\int_0^x \exp(-\int_t^x \frac{\lambda(s)}{\varepsilon + p(s)} ds)\lambda(t)\frac{\varphi(x) - \varphi(t)}{\varepsilon + p(t)} dt +$$

$$+ \frac{1}{\varepsilon + p(x)}\varphi(x)\exp(-\int_0^x \frac{\lambda(s)}{\varepsilon + p(s)} ds)$$

$$\sqrt{n}]d_1^{-1}(L_K + C_0K_1)\int_0^x \|\eta_\varepsilon(t)\| dt$$

Consequently, using estimations from (11), we obtain

$$\|\eta_\varepsilon(x)\| \le C_3 d_1^{-1}(L_K + C_0K_1)\int_0^x \|\eta_\varepsilon(t)\| dt + \|\varepsilon(H_\varepsilon\upsilon)(x)\|_{C_n}.$$

From this, using Gronuoll-Bellman's inequality and lemma 2, we obtain the estimation (9). Thus from (9) and (10) follows uniform convergence $\upsilon_\varepsilon(x) \to \upsilon(x)$, $\varepsilon \to 0$. QED

Corollary. If conditions *a)-b)*, (4) are fulfilled then the system (1) has unique solution in the space $C_n^\gamma[0,b]$, $0 < \gamma \le 1$.

Lemma 3. If conditions *a)-b)*, Eq. (4), $\upsilon(x) \in C_n[0,b]$, $\|G(x)\| \le C_1\lambda(x)$ are fulfilled, then the following estimate takes place

$$\|\varepsilon(H_\varepsilon\upsilon)(x)\|_{C_n} \le$$

$$[2((e\theta_2)^{-1}C_1 + \varepsilon^{\beta_0})\|\upsilon(x)\|_{C_n}\varepsilon^{1-\beta_0} + C_1\omega(\varepsilon^{\beta_0})]\sqrt{n}, \qquad (12)$$

where

$$\omega_{\bar{u}}(\bar{\varepsilon}) = \sup_{|z-\zeta| \le \bar{\varepsilon}} \{ \|\upsilon(\varphi^{-1}(z)) - \upsilon(\varphi^{-1}(\zeta))\| / z, \zeta \in [0, \varphi(b)]\},$$

$0 < \beta_0 < 1$,

and $\varphi^{-1}(z)$ -inverse function to $\varphi(x)$.

Proof. Using the equality (8), taking into account estimations (4) and (6) we obtain

$$\frac{\varepsilon}{\varepsilon + p(x)}\exp(-\int_0^x \frac{G(s)ds}{\varepsilon + p(s)})\|\upsilon(x) - \upsilon(0)\| \le$$

$$\frac{2\varepsilon}{\varepsilon + p(0)}\|\upsilon(x)\|_{C_n}\sqrt{n}. \qquad (13)$$

Let $0 \le x \le \varphi^{-1}(\varepsilon^{\beta_0})$, $0 < \beta_0 < 1$. From this we get $0 \le z \le \varepsilon^{\beta_0}$, $z = \varphi(x)$, $|z\text{-}\zeta| \le \varepsilon^{\beta_0}$, $\zeta = \varphi(t)$. We have

$$\frac{\varepsilon}{\varepsilon + p(x)}\int_0^x \exp(-\int_t^x \frac{G(s)ds}{\varepsilon + p(s)})\frac{G(t)}{\varepsilon + p(t)}$$

$$\|\upsilon(x) - \upsilon(t)\| dt \le C_1\sqrt{n}\omega(\varepsilon^{\beta_0}) \qquad (14)$$

We use the properties of function $p(x)$ and denotation $\sigma = \varphi^{-1}(\varphi(x) - \varepsilon^{\beta_0})$ for x: $\varphi^{-1}(\varepsilon^{\beta_0}) \le x \le b$. Thus

$$\frac{\varepsilon}{\varepsilon + p(x)}\int_0^x \exp(-\int_t^x \frac{G(s)ds}{\varepsilon + p(s)})\frac{G(t)}{\varepsilon + p(t)}\|\upsilon(x) - \upsilon(t)\| dt =$$

$$\frac{\varepsilon}{\varepsilon + p(x)}C_1\sqrt{n} \times$$

$$\times[\int_0^\sigma \exp(-\int_t^x \frac{\lambda(s)ds}{\varepsilon + p(s)})\frac{\lambda(t)}{\varepsilon + p(t)}\|\upsilon(x) - \upsilon(t)\| dt +$$

$$\int_\sigma^x \exp(-\int_t^x \frac{\lambda(s)ds}{\varepsilon + p(s)})\frac{\lambda(t)}{\varepsilon + p(t)} \times$$

$$\times\|\upsilon(x)-\upsilon(t)\|dt]\le$$

$$[2\frac{\varepsilon}{\varepsilon+p(x)}\|\upsilon(x)\|_{C_n}(\exp(-\int_{\sigma}^{x}\frac{\lambda(s)ds}{\varepsilon+p(s)})-$$

$$\exp(-\int_{0}^{x}\frac{G(s)ds}{\varepsilon+p(s)}))+$$

$$+\omega(\varepsilon^{\beta_0})]C_1\sqrt{n}\le$$

$$[2\frac{\varepsilon}{\varepsilon+p(x)}\|\upsilon(x)\|_{C_n}\exp(-\int_{\sigma}^{x}\frac{\lambda(s)ds}{\varepsilon+p(s)})+$$

$$\omega(\varepsilon^{\beta_0})]C_1\sqrt{n}\le$$

$$\le[2\|\upsilon(x)\|_{C_n}\frac{\varepsilon}{\varepsilon+p(\sigma)}\exp(-\frac{\theta_2\varepsilon^{\beta_0}}{\varepsilon+p(\sigma)})$$

$$+\omega(\varepsilon^{\beta_0})]C_1\sqrt{n}\le[2(e\theta_2)^{-1}\|\upsilon(x)\|_{C_n}\times$$

$$\times\varepsilon^{1-\beta_0}+\omega(\varepsilon^{\beta_0})]C_1\sqrt{n}\,. \qquad (15)$$

Combining estimates (13)-(15) we obtain (12). QED

Theorem 2. Let conditions *a)-b)*, (4), $\|G(x)\|\le C_1\lambda(x)$ take place and system (1) has a solution $\upsilon(x)\in C_n[0,b]$. Then the solution of (3) uniformly converges to the solution of system (1), when $\varepsilon\to 0$, and

$$\|\upsilon_\varepsilon(x)-\upsilon(x)\|_{C_n}\le$$

$$[2(C_1(e\theta_2)^{-1}+\varepsilon^{\beta_0})\|\upsilon(x)\|_{C_n}\varepsilon^{1-\beta_0}+C_1\omega(\varepsilon^{\beta_0})]\sqrt{n}d_4,$$

$$d_4=\exp(C_3b(L_K+K_1)/d_1),$$

$$C_3=[2\theta_2^{-2}C_1+\|\varphi(x)\|_C/p(0)]\sqrt{n},\ 0<\sigma<1,$$

$$\omega_u(\bar{\varepsilon})=\sup_{|z-\zeta|\le\bar{\varepsilon}}\{\|\upsilon(\varphi^{-1}(z))-\upsilon(\varphi^{-1}(\zeta))\|/z,\zeta\in[0,\varphi(b)]\},$$

$\varphi^{-1}(z)$ -inverse function to $\varphi(x)$.

Corollary. If conditions *a)-b)*, (4) are fulfilled then the equation (1) has unique solution in space $C_n[0,b]$.

Thus it is proved that Lavrentiev method is applicable to linear system of the third-kind Volterra equations.

Regularization of the Non-Linear System

The regularization of a non-linear equation is much more complicated. We applied the Lavrentiev method to particular form of a Kernel of integral.

Let $N(x,t,\upsilon)=K(x,t)+M(x,t,\upsilon)$, where $K(x,t)$ is a matrix-valued function, satisfying the condition *a),* vector-valued function $M(x,t,\upsilon)\in C_n^{0,0,1}(D\times R^n)$ and

$$M_\upsilon(x,t,\upsilon)\in Lip(x|L_M),\ M(x,t,0)=0,$$
$$0<L_M=const. \qquad (16)$$

A system of non-linear Volterra integral equation of the third kind

$$p(x)\upsilon(x)+\int_0^x N(x,t,\upsilon(t))dt=f(x) \qquad (17)$$

is equivalent to the system

$$(A\upsilon)(x)+(G\upsilon)(x)=(\Phi\upsilon)(x)+g(x), \qquad (18)$$

where

$$(\Phi\upsilon)(x)=\int_0^x\Phi(x,t,\upsilon(t))dt,$$

$$\Phi(x,t,\upsilon(t))=[K(t,t)-K(x,t)]\upsilon(t)-M(x,t,\upsilon(t))-$$

$$-C_0\int_t^x M(v,t,\upsilon(t))dv;$$

Operators *A, G* and function *g(x)*are defined by (2). The proof of equivalence is the same as in Lemma 1.

Theorem 3. Let conditions *a)*, (4), (16), $\|G(x)\|\le C_1\lambda(x)$ are fulfilled, and system (17) has a solution $\upsilon(x)\in C_n^\gamma[0,b]$, $0<\gamma\le 1$. Then the solution of the system

$$(\varepsilon I+A)\upsilon_\varepsilon(x)+(G\upsilon_\varepsilon)(x)=(\Phi\upsilon_\varepsilon)(x)+\varepsilon\upsilon(0)+g(x) \quad (19)$$

uniformly converges to the solution of system (17) with $\varepsilon \to 0$, and following estimation takes place

$$\|\upsilon_\varepsilon(x)-\upsilon(x)\|_C \le d_3\varepsilon^\gamma,$$
$$d_0 = \sup_{(x,s)\in[0,b]}\{\|\upsilon(x)-\upsilon(s)\|/|x-s|^\gamma\},$$
$$d_3 = d_0\sqrt{n}\exp(C_4C_3)(C_1\theta_2^{-(1+\gamma)}d_2d_1^{-\gamma} + $$
$$+p_0^{-1}\varepsilon^{1-\gamma}b^\gamma),$$
$$C_4 = d_1^{-1}[L_K + C_0K_1 + (1+C_0)(L_M+K_M)],$$
$$K_M = \max_{\Omega_0\times R^n}\|M_\upsilon(x,t,\upsilon)\|.$$

Proof. Let the conditions of the theorem 3 and the following estimations be fulfilled

$$\|(L\upsilon)(x)-(L\upsilon)(t)\| \le 2d_1^{-1}(L_K + C_0K_1)(\varphi(x)$$
$$-\varphi(t))\|(J_0\upsilon)(x)\|$$
$$\|(M\upsilon)(x)-(M\upsilon)(t)\| \le$$
$$\|\int_0^t[M(x,v,\upsilon(v))-M(t,v,\upsilon(v))]dv +$$
$$\int_t^x M(x,v,\upsilon(v))dv\| + \|C_0\int_0^t\int_t^x[M(v,s,\upsilon(s))dvds +$$
$$+C_0\int_t^x\int_s^x M(v,s,\upsilon(v))dvds\| \le 2d_1^{-1}[(L_M+K_M)(1+C_0)\times$$
$$\times(\varphi(x)-\varphi(t))\|(J_0\upsilon)(x)\|,\ (J_0\upsilon)(x) = \int_0^x\upsilon(t)dt.$$

Then the following estimation is fulfilled for the nonlinear operator $(\Phi\upsilon)(x)$

$$\|(\Phi\upsilon)(x)-(\Phi\upsilon)(t)\| \le 2C_4(\varphi(x)-\varphi(t))\|(J_0\upsilon)(x)\|.$$

If the condition (4) and an inequality $\|G(x)\| \le C_1\lambda(x)$ take place, then the estimation

$$\|(H_\varepsilon[\Phi\upsilon])(x)\| \le C_4C_3\|(J_0\upsilon)(x)\|,$$
$$C_3 = (2C_1\theta_2^{-2} + \|\varphi(x)\|_C / p(0))\sqrt{n} \qquad (20)$$

is fulfilled.

Consequently, using the substitution (10) and estimation (20), we can prove the Theorem 3. QED

Corollary. If conditions *a)*, (4), (16) and the inequality $\|G(x)\| \le C_1\lambda(x)$ are fulfilled then the equation (17) has a unique solution in $C_n^\gamma[0,b]$, $0<\gamma\le 1$.

Theorem 5. Let conditions *a*, (4), (16) $\|G(x)\| \le C_1\lambda(x)$ be fulfilled and (17) has a solution $\upsilon(x)\in C_n[0,b]$. Then the solution of the system (19) uniformly converges to the solution of the system (17), with $\varepsilon\to 0$, and following estimation takes place

$$\|\upsilon_\varepsilon(x)-\upsilon(x)\|_{C_n} \le$$
$$[2(C_1(e\theta_2)^{-1} + p_0^{-1}\varepsilon^{\beta_0})\|\upsilon(x)\|_C\varepsilon^{1-\beta_0} + C_1\omega(\varepsilon^{\beta_0})]\sqrt{n}d_4,$$
$$d_4 = \exp(C_3C_4),$$
$$\omega_{\bar u}(\bar\varepsilon) = \sup_{|z-\zeta|\le\bar\varepsilon}\{\|\upsilon(\varphi^{-1}(z))-\upsilon(\varphi^{-1}(\zeta))\| / z,\zeta\in[0,\varphi(b)]\},$$
$$0<\beta_0<1,$$

where $\varphi^{-1}(z)$ is the inverse function to $\varphi(x)$.

Corollary. If conditions *a)*, (4), (16), $\|G(x)\| \le C_1\lambda(x)$ are fulfilled then the system (17) has a unique solution in the space $C_n[0,b]$.

Results

From the above it follows that scheme (3) and (19) are the Volterrian regularizations under certain conditions, giving uniform approximation to the exact solution of the Volterra integral equation of the third kind. The Volterra operator has no singular point and it gives us opportunity to apply numerical iteration method to get an approximate solution.

Figure 1 shows exact solution $\upsilon=xe^{-x}$ of equation (1) with $n=1$, $K(x,t)=(2x+4)exp(t-x)$, $p(x)=4-x^2$, $f(x)=x(2x+4)e^{-x}$ and solution of (3)

with two values of parameter $\varepsilon=0{,}316228$ ($h=0.1$), $\varepsilon=0{,}223607$ ($h=0.05$). The following evaluation scheme was applied

$$\upsilon_{\varepsilon,i} = -\frac{1}{\varepsilon + p_i} h\sum_{j=1}^{i} W_{i,j}^{\varepsilon,h} G_j [h\sum_{k=1}^{j} L_{j,k}\upsilon_{\varepsilon,k}$$

$$-h\sum_{k=1}^{i} L_{i,k}\upsilon_{\varepsilon,k} + g_j - g_i] + \tilde{W}_{i,1}^{\varepsilon,h}[h\sum_{j=1}^{i} L_{i,j}\upsilon_{\varepsilon,j} +$$

$$+g_i + \varepsilon\upsilon_0]\}, \; i=1..n, \; \varepsilon = h^{\alpha}, \; \alpha=0{,}3, \; \upsilon_0 = \upsilon(0),$$

where $L_{j,k} = L(x_j, x_k)$, $\upsilon_{\varepsilon,j} = \upsilon_{\varepsilon}(x_j)$, $g_i = g(x_i)$, $p_i = p(x_i)$, $x_j = jh$, $j=1..i$,

$$L(x_i, x_k) = -K(x_i, x_k) + K(x_k, x_k) - C_0 h \sum_{m=k+1}^{i} K(x_m, x_k),$$

$C_0=0{,}1$, $i=1..n$,

$$W_{i,j}^{\varepsilon,h} = \frac{1}{\varepsilon + p_j} \exp\left(-h\sum_{m=j}^{i} \frac{G_m}{\varepsilon + p_m} \right),$$

$$\tilde{W}_{i,1}^{\varepsilon,h} = \frac{1}{\varepsilon + p_0} \exp\left(-h\sum_{m=1}^{i} \frac{G_m + p'_m}{\varepsilon + p_m} \right), \; i=1..n.$$

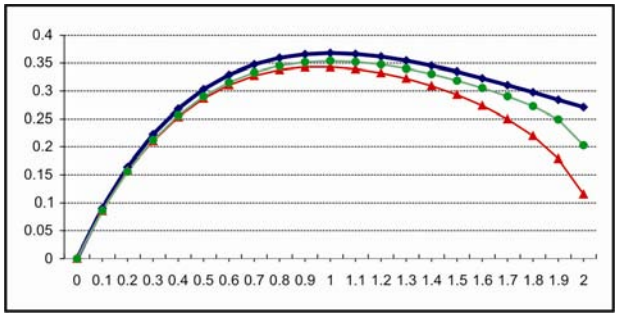

Figure 1. ♦– plot of the exact solution, ▲-approximate solution with *(0.1 0.2 ε=0,316228 h=0,1)*, •- Fig.1. ♦– plot of the exact solution, ▲-approximate solution with *ε=0,316228* (*h=0,1*), •- approximate solution with *ε=0,223607* (*h=0.05*).

Let us note that in this example the condition *a)* is fulfilled for $K(x,t)$, $p(x)$, $f(x)$ and the condition (4) with $C_0=0{,}1$, $\theta_1 = 0.7$ .The present results can be used for investigating of a wide class of differential equations, inverse and non-local boundary problems for partial differential equations.

Discussion

This paper is close by ideology to [6]. In [6] was used the property of non-decreasing function $p(x)$. In the case of non-increasing function $p(x)$, the lemmas of [6] are not fulfilled. Because of this difficulty we shifted to equivalent system (2) to get regularization of Eq. (1). Additionally, we needed the differential property of $p(x)$ in the form of inequality (8). The above investigated method of regularization (3) takes place also for the third-kind Volterra equations with non-decreasing function if the kernel of operator is not vanished at the beginning of the matrix diagonal. However, the regularization scheme [6] is not applicable in this case. Therefore, we have an opportunity to solve the system (1) when $p(x)$ vanishes at internal point of interval, e.g. if $p(c) = 0, 0 < c < b$, and $p(x)$ is non-decreasing on *[0, c]*, and $p(x)$ is non-increasing on *[c,b]*. Then we regularize the system (1) on the portion *[0,c]* by the scheme of [6], and regularize (1) on *[c,b]* according to the scheme of the present work.

One may move on to apply the findings of the present study to the case of Kernel $K(x,t)$ integrable by variable t. Furthermore, it would be interesting to consider the case of integration on positive semiaxis $x > 0$. We would like to point out that there are no positive research results of regularization of the third-kind Volterra equation in the space of integrable functions.

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SPECTROPHOTOMETRIC DETERMINATION OF SULPIRIDE IN PURE FORM AND PHARMACEUTICAL PREPARATIONS

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Abstract: Sulpiride reacts with chloranil to give a green coloured complex after heating for 100s at 100°C having maximum absorbance at 590nm. The reaction is selective for sulpiride with 0.01 mg/10 ml as visual limit of quantitation and provides a basis for a new spectrophotometric determination. The reaction obeys Beer's Law from 0.01 to 3.5 mg/10 ml of sulpiride and the relative standard deviation is 0.68 %. The quantitative assessment of tolerable amounts of other drugs not interfering has also been studied.

Keywords: Sulpiride, 1,4 dioxane, pharmaceutical analysis.

Introduction

Sulpiride is the 5-sulphamoyl-N-[(1-ethylpyrrolidine-2-yl)methyl]-2-methoxy benzamide (Fig. 1). It is commonly used as an antipsychotic and antidepressant drug. It has an antiemetic action and inhibits gastrin secretion. It is used for neurosis, migrain pain and functional intestinal spasms. The most common side effects of sulpiride are sedation, drowsiness, dizziness, depression, headache, restlessness and impaired concentration. Parkinsonian symptoms appear with higher doses, alongwith acute dystonias, akathisia and tardive dyskinesia, cholestatic jaundice, blurred vision, xerosronia and diaphoresis of skin [1].

Many analytical techniques have been employed for the determination of sulpiride. In HPLC [2,3], ion pair reversed phase HPLC [4] reversed phase HPLC [5] and HPTLC scanning densitometry [6] procedures, the extract from 1 ml of plasma was dissolved in methylene chloride and sulpiride was back extracted with 0.01 M hydrochloric acid [3]. To compensate the loss of sulpiride during extraction procedure an internal standard very similar in chemical structure and UV absorbance to those of sulpiride was used and the RSD value was high i.e. 5.1 % [5]. In the voltammetric procedure the voltammetric response strongly depended upon the pH of the medium [7]. Three procedures are described simultaneously for the assay of mebeverine and sulpiride viz first derivative UV spectrophotometry, TLC-densitometry and reversed phase HPLC [8]. In the first derivative UV spectrophotometry the first derivative amplitudes at 214.2 and 221.6 nm were selected for the assay of mebeverine and sulpiride respectively. While in the TLC procedure the separation of both the drugs was carried out prior to densitometric measurement and for the third procedure (HPLC) the separation was carried out on a reversed phase Bondapak CN column and buclizine was used as an internal standard. In the derivative spectrophotometry [9,10] the first order derivative was carried out at wavelengths 275 and 300 nm [9] and by applying zero crossing technique measurement [10]. In the

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capillary electrophoresis procedures [11,12] statistical analysis of numerous experiments performed under identical conditions reveal a loose correlation of the migration separation factor with the migration retardation factor [12]. Long and tedious procedures were carried out by electrokinetic chromatography [13] and oscillopolarography [14].

During the systematic study of drugs of abuse it was found that sulpiride reacts with chloranil to give a green coloured complex having a maximum absorbance at 590 nm. The reaction obeys Beer's Law and has 0.01 mg/10 ml as visual limit of quantitation. The present method is simple, accurate, precise and sensitive. Percentage of tolerable limits of other drugs not interfering are also studied.

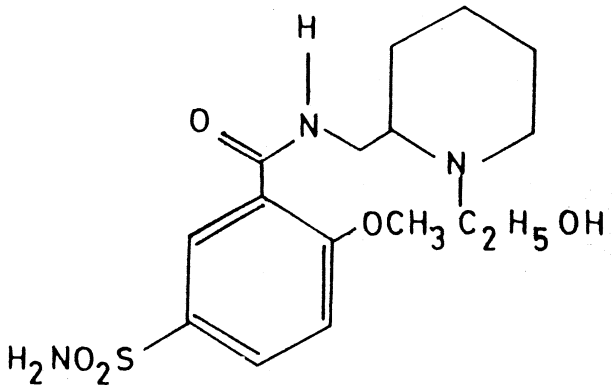

Figure 1. Structural formula of sulpiride.

Materials and Methods

Apparatus and reagents

Hitachi U-1100 spectrophotometer with 1 cm silica cells was used to measure the absorbance. Analytical grade chemicals and doubly distilled water were used. Sulpiride (Pacific Pharma, Lahore, Pakistan) standard solution (w/v) 1 mg/ml was prepared by dissolving 100 mg in 100 ml of 1,4 dioxane (BDH) to get a stock solution, which was diluted further as required. A 2 % (w/v) chloranil (Fluka USA) solution was prepared by dissolving 2 g of chloranil in 100 ml of 1,4 dioxane.

General procedures

To an aliquot of sulpiride containing 0.01 to 3.5 mg/10 ml 2 ml of 2% chloranil solution was added and the contents were heated for 100s in a water bath at 100°C. The contents were cooled to room temperature and the volume was made up to 10 ml with 1,4 dioxane. The resulting absorbance was measured at 590 nm, employing all reagents except sulpiride as a blank. The experiment was repeated with different volumes of standard sulpiride solution and a calibration curve was prepared (Fig. 2). The colour reaction obeys Beer's Law from 0.01 to 3.5 mg/10 ml of sulpiride.

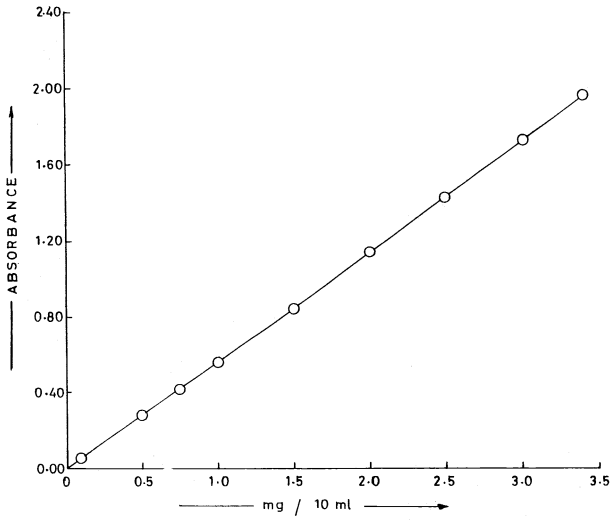

Figure 2. Calibration curve of sulpiride with chloranil.

Procedure for studying the interfering compounds

To an aliquot containing 1 mg/ml of sulpiride different amounts of various organic compounds (1 mg/ml) (w/v) were added individually as long as the solution showed the same (±0.01) absorbance as that of pure sulpiride solution without the addition of the interfering organic compound, under experimental conditions, as described in the general procedure.

Procedure for the determination of sulpiride in pharmaceutical preparations

Tablets containing 50 mg and 100 mg of sulpiride were powdered, weighed, dissolved in 1,4

dioxane and filtered. The filtrate was diluted with 1,4 dioxane to get a 1 mg/ml solution of sulpiride. An aliquot containing 0.01 to 3.5 mg/10 ml was taken, the procedure was followed as described above and the absorbance was measured at 590 nm. The quantity per tablet was calculated from the standard calibration curve.

Results and Discussion

Absorption spectrum of the coloured complex

Sulpiride reacts with chloranil when heated for 100s at 100°C to give a green coloured complex, the absorption spectra of which under the optimum condition lies at 590 nm (Fig. 3). Hence all measurements for further studies were carried out at this wavelength.

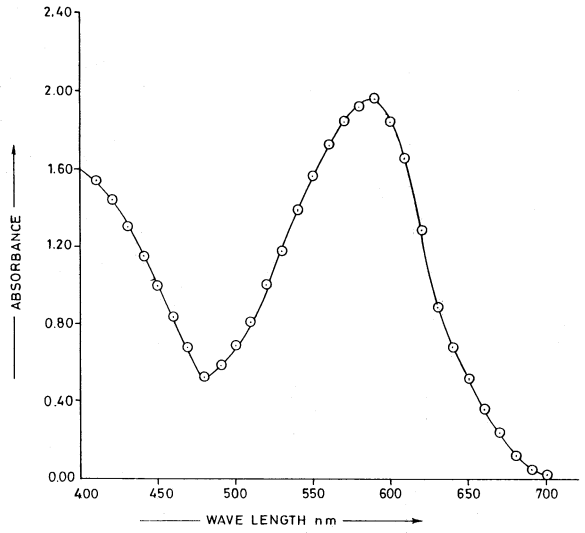

Figure 3. Absorption spectra of sulpiride with chloranil.

Effect of colour producing reagent

Chloranil was used as colour producing reagent. It was found that 40 mg/10 ml of chloranil gave maximum colour (Fig. 4) above and below this concentration the colour intensity diminished and the colour became unstable. The probable mechanism is that chloranil as an oxidizing agent reacts with the sulfonamine group of sulpiride which in turn directly transfers an electron to chloranil thus forming a green coloured complex. Other antipsychotic drugs like chlorpromazine and prochlorperazine do not form any coloured complex with chloranil because their reactive sites are tertiary amines which are ordinarily not reactive enough for this reaction [15].

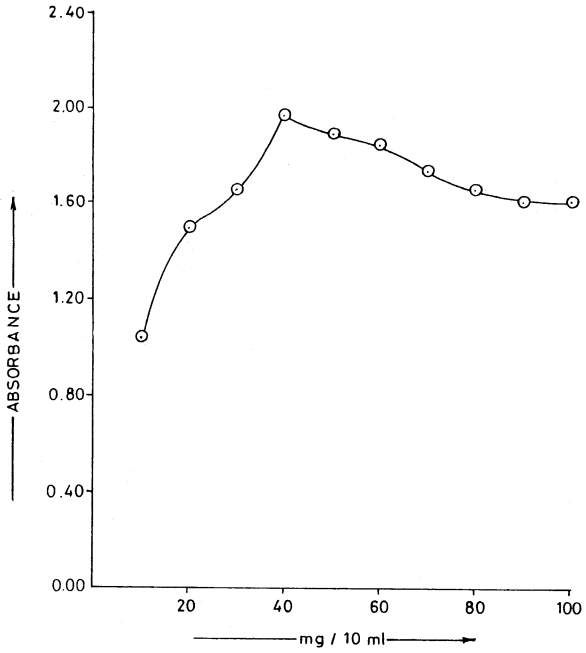

Figure 4. Effect of chloranil.

Effect of temperature and heating time

The effect of temperature is shown in Fig. 5. It was found that with the rise of temperature the colour intensity increased and was maximum and stable at 100°C. The colour did not develop at room temperature. The absorbance of the developed colour remained stable for more than 24 h. A water bath was used to carry out the temperature studies. After the production of the colour the contents of the test tube were cooled to room temperature prior to dilution with 1,4 dioxane and measurement of absorbance. The effect of heating time on colour intensity is shown in Fig. 6. It was found that heating for 100s at 100°C gave maximum colour. Above and below these timings the colour intensity was less and also unstable.

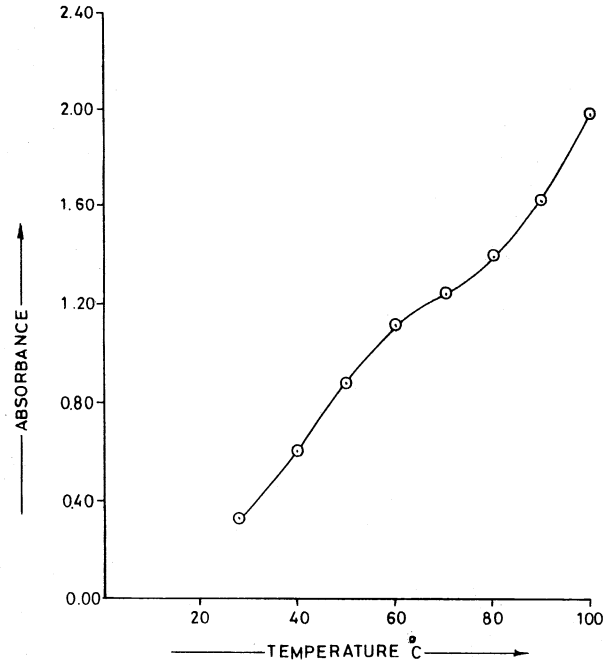

Figure 5. Effect of temperature.

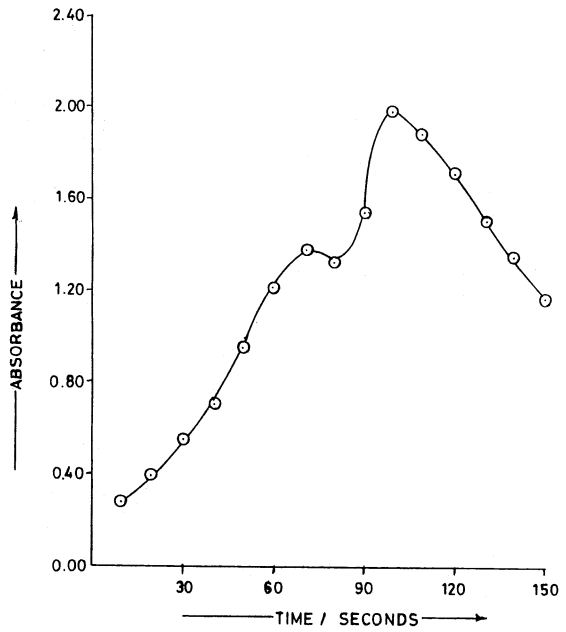

Figure 6. Effect of heating time.

Effect of organic solvents

Different organic solvents such as dichloromethane, benzene, hexane, chloroform, methyl ethyl ketone, tetrahydrofuran, carbontetrachloride and trichlorobenzene, were tested for colour extraction and stability. Since none were effective therefore no solvent was employed except for dioxane which was used for dilution and stability of the coloured complex.

Sensitivity

The results for the determination of sulpiride are shown in Tables 1 and 2, which show the sensitive, validity and repeatability of the method. It is reasonably precise and accurate, as the amount taken for identical sample is known and the amount found by the above procedure does not exceed the relative standard deviation of 0.68% which is the replicate of five independent measurements (cf. Table 1). The calibration graph is linear in the range of 0.01 to 3.5 mg/10 ml. The apparent molar absorptivity calculated was 0.1921 x 10^4 mol^{-1} cm^{-1} and the regression equation [16] was calculated by the method of least squares from twelve points each of which was the average of five determinations. The correlation between absorbance and concentration is 0.999 in terms of correlation coefficient (r).

Table 1. Determination of sulpiride from pure solution.

Sulpiride taken mg/10ml	Sulpiride found * mg/10ml	Relative Standard Deviation %
0.100	0.102	0.04
0.200	0.203	0.50
0.500	0.504	0.31
1.000	1.042	0.15
1.500	1.515	0.68
2.000	2.017	0.50
2.500	2.512	0.67
3.000	3.022	0.49
3.500	3.505	0.35

*Every reading is an average of five independent measurements.

Table 2. Optical characteristics prevision and accuracy of the proposed method.

Parameters	Values
λ_{max} (nm)	590
Beer's Law \Limits (mg/10 ml, C)	0.01 - 3.5
Molar absorptivity (mol^{-1} cm^{-1})	0.1921×10^4
Limit of Detection (mg/10 ml)	0.01
Regression Equation (Y)*	
Slope (b)	0.60
Intercept (a)	0.006
Correlation coefficient (r)	0.999
Relative standard deviation at 1.5 mg/10 ml (RSD%)**	0.68
%Range of error (confidence limits) at 95% confidence level	50.10±0.01

*Y = a + bC, where C is the concentration of analyte (mg/10 ml) and Y is the absorbance unit.
**Calculated from five independent measurements.

Interferences

The quantitative assessment of different organic compounds (w/v) under the experimental conditions is given in Table 3. Various amounts of diverse interfering compounds having similar actions were added to fixed amount of sulpiride (1 mg/ml) and the recommended procedure for the spectrophotometric determination was followed. Other compounds which are common interferences and have similar action like chlorpromazine, prochlorperazine, naproxen, fluoxetin and atenolol did not interfere.

Table 3. Quantitative assessment of tolerable amount of other drugs.

Drugs	Maximum Amount Not Interfering* (%)
Prochlorperazine	250
Chlorpromazine HCl	400
Chlorophenarmine maleate	280
Dextromethorphane HBr	200
Triprolidine HCl	200
Benzodiazepines	260
Thioridazine	300
Ibuprofen	350
Metoclopramide HCl	180
Aldomet	260
Haloperidol	240
Methyldopa	300
Phenytoin Sodium	310
Cyclizine HCl	200
Fluoxetine	200
Atenolol	250
Naproxen	310
Indomethacin	290
Dextropropoxyphene HCl	325
Amitriptyline HCl	275

*The value is the percentage of the drug with respect to 1mg/10ml of sulpiride that causes +0.01 changes in absorbance.

Application

The proposed method is successfully applied for the quality control of pure sulpiride and in the pharmaceutical dosage form as shown in Table 4. The excipients used in formulation did not interfere with the analysis.

The spectrophotometric method for the determination of sulpiride is reliable, simple, sensitive and reproducible. It is selective for sulphiride. The method can be successfully applied to the micro determination of sulpiride either in pure form or in pharmaceutical preparations. The colour reaction has 0.01 mg/10 ml as visual limit of quantitation. The advantage of the present procedure is that it does not require many reagents nor solvents and has a low RSD value (0.68 %) whereas the HPLC [3,4] procedures are long, tedious and expensive involving many reagents and solvents showing RSD values of 2.29 % [4] and 5 % [5]. The literature indicates that this colour reaction has not been reported previously. Drugs like benzodiazepines, chlorpromazine, prochlorperazine, haloperidal and ibuprofen do not interfere. A significant advantage of a spectrophotometric determination is its application to the determination of individual compounds. This aspect of spectrophotometric analysis is of major interest in the analytical pharmacy, since it offers a distinct possibility of quality control in the assay of pharmaceutical dosage formulation.

Table 4. Determination of sulphiride from pharmaceutical preparations.

Drug	Trade Name	Pharmaceutical Preparation	Amount Present (Manufacturer's Specifications) (mg)	Amount Found*	Percentage Recovery
Sulpiride	Levopraid (Pacific Pharmaceutical, Lahore Pakistan)	Tablet	50.00	50.00	100.00
Sulpiride	Levopraid (Pacific Pharmaceutical, Lahore Pakistan)	Tablet	100.00	99.95	99.99

*Every reading is an average of five independent measurements

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FLOW OF A VISCOUS FLUID DUE TO NON-COAXIAL ROTATIONS OF TWO DISKS

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Abstract: The flow between two non-coaxially rotating disks has been considered. The velocity field is obtained between the two disks, which are initially at rest and then start rotating with respect to different axes of rotation. The velocity field is obtained analytically using eigenfunction expansion method.

***Keywords*:** Unsteady viscous fluid, non-coaxial rotations, eigenfunction expansion method.

Introduction

The unsteady flow due to non-coaxial rotations of a disk and a fluid at infinity has been a subject of great interest for many scientists, researchers and engineers. It has attracted a large number of experimentalists as the solutions of many practical rotating flow problems lie in the understanding of the behaviour of unsteady boundary layers. Mention may be made to the interesting works in the references [1 – 8].

The unsteady flow due to non-coaxial rotations of a disk executing oscillations in its own plane and a fluid at infinity has been investigated by Kasiviswanathan and Rao [2]. The unsteady flow due to eccentric rotations of a disk and the fluid at infinity, which are impulsively started was studied by Pop [3], he assumed that the flow is two-dimensional and both the disk and the fluid at infinity are initially at rest and that they are impulsively started at time zero. Later on, it was pointed out by Erdogan [4] that under the assumed conditions of Pop [3], the flow becomes three-dimensional and is perhaps not very simple to handle. Erdogan [4] however, suggested a change in the initial condition and proposed that the disk and the fluid are initially rotating about $z' - axis$ and suddenly sets in motion, the disk is rotating about $z - axis$ and fluid about

$z' - axis$. He [4] considered that the problem is two-dimensional and presents an analytical solution for the velocity field. We have presented here, the analytical solution for the problem in which the fluid does not extend to infinity but remains confined between two disks at z=0 and z=d. Initially the two disks at z=0 and z=d are at rest and then suddenly starts rotating about z and $z' - axis$ respectively. It has been found that the problem is solvable by keeping the initial condition (the disk and the fluid remains initially at rest) and changing the fluid from infinity to the disk at z=d. The eigenfunction expansion method has been used to solve the governing equation with non-homogenous boundary conditions. Perhaps this is for the first time that this method is applied in finding the analytical solution of partial differential equations arising in vibration of disks/plates in Newtonian fluid. The problem is interesting from both application and mathematical points of view.

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Mathematical formulation

Consider an unsteady flow of a viscous fluid between two parallel disks rotating with the same constant angular velocity Ω about two non-coincident axes, separated by a distance l. From Pop [3], Erdogan [4] and Hayat *et al.* [5], we assume the velocity field of the form

$$u = -\Omega y + f(z,t),\ \ v = \Omega x + g(z,t) \tag{1}$$

with the following boundary and initial conditions

$$\begin{aligned} &u = v = w = 0 \quad \text{for } 0 \le z \le d,\ t \le 0,\\ &u = -\Omega y,\ \ v = \Omega x,\ \ w = 0 \text{ at } z = 0,\ t > 0,\\ &u = -\Omega y + \Omega l,\ \ v = \Omega x \text{ at } z = d,\ t > 0, \end{aligned} \tag{2}$$

where d is the distance between the two disks and u, v and w are the components of the velocity. Making use of equation (1) in the Navier-Stokes equations, we obtain

$$\begin{aligned} &\frac{1}{\rho}\frac{\partial p}{\partial x} = \Omega^2 x + \left(\nu\frac{\partial^2 f}{\partial z^2} - \frac{\partial f}{\partial t} + \Omega g\right),\\ &\frac{1}{\rho}\frac{\partial p}{\partial y} = \Omega^2 y + \left(\nu\frac{\partial^2 g}{\partial z^2} - \frac{\partial g}{\partial t} - \Omega f\right),\\ &\frac{1}{\rho}\frac{\partial p}{\partial z} = 0. \end{aligned} \tag{3}$$

The conditions in terms of f and g are

$$\begin{aligned} &f(0,t) = g(0,t) = 0, && \text{for } t > 0,\\ &f(d,t) = \Omega l,\ \ g(d,t) = 0 && \text{for all } t \end{aligned} \tag{4}$$

and

$$f(z,0) = \Omega y,\ \ g(z,0) = -\Omega x, \qquad \text{for } 0 < z < d. \tag{5}$$

From equation (3), $p = p\,(x, y, t)$, thus differentiation $\partial p/\partial x$ and $\partial p/\partial y$ of equation (3) with respect to z and then using boundary conditions (4), we have

$$\nu\frac{\partial^2 F}{\partial z^2} - \frac{\partial F}{\partial t} - i\Omega F = 0, \tag{6}$$

in which

$$F = \frac{f}{\Omega l} + i\frac{g}{\Omega l} - 1 \tag{7}$$

and the initial and boundary conditions (4) and (5) take the form

$$\begin{aligned} &F(0,t) = -1,\ \ F(d,t) = 0,\\ &F(z,0) = \left(\frac{y}{l} - \frac{ix}{l} - 1\right). \end{aligned} \tag{8}$$

Introducing

$$F(z,t) = H(z,t)e^{-i\Omega t},$$

The initial value problem (6) and (8) reduces to

$$\nu\frac{\partial^2 H}{\partial z^2} - \frac{\partial H}{\partial t} = 0, \tag{9}$$

$$H(0,t) = -e^{i\Omega t},\ \ H(d,t) = 0,$$

$$H(z,0) = \left(\frac{y}{l} - \frac{ix}{l} - 1\right). \tag{10}$$

Solution of the problem

We look for the solution of this problem by the method of eigenfunction expansion. For that we write

$$H(z,t) = r(z,t) + \psi(z,t). \tag{11}$$

Inserting equation (11) into equation (9) and conditions (10), we find that $\psi(z, t)$ satisfies

$$\nu\frac{\partial^2 \psi}{\partial z^2} - \frac{\partial \psi}{\partial t} = i\Omega e^{i\Omega t}\left(\frac{z}{d} - 1\right), \tag{12}$$

subject to the conditions

$$\psi(0,t) = 0,\ \ \psi(d,t) = 0 \tag{13}$$

and

$$\psi(z,0) = \left(\frac{y}{l} - \frac{ix}{l} - \frac{z}{d}\right), \tag{14}$$

where

$$r(z,t) = e^{i\Omega t}\left(\frac{z}{d} - 1\right). \tag{15}$$

The solution of non-homogenous partial differential equation (12) with initial and boundary conditions (13) to (15) by eigenfunction expansion method is given as

$$\psi(z,t)=\sum_{n=1}^{\infty}a_n(t)\sin\left(\frac{n\pi}{d}\right)z, \tag{16}$$

where

$$a_n(t)=a_n(0)\exp\left[\left(\frac{n\pi}{d}\right)^2 vt\right]- \frac{2i\Omega}{n\pi\left(i\Omega+v\left(\frac{n\pi}{d}\right)^2\right)}\left(e^{i\Omega t}-e^{-\left(\frac{n\pi}{d}\right)^2 vt}\right), \tag{17}$$

$$a_n(0)=\frac{2}{n\pi}\left(\frac{y}{l}-\frac{ix}{l}\right)\left(1-(-1)^n\right)+\frac{2}{n\pi}(-1)^n. \tag{18}$$

From equations (11), (15) and (16), we obtain

$$H(z,t)=e^{i\Omega t}\left(\frac{z}{d}-1\right)+\sum_{n=1}^{\infty}a_n(t)\sin\left(\frac{n\pi}{d}\right)z. \tag{19}$$

We note that all the boundary and initial conditions are satisfied by the solution. The above solution can also be written as

$$\frac{f}{\Omega l}+i\frac{g}{\Omega l}=\frac{z}{d}+\sum_{n=1}^{\infty}\left[\begin{array}{l}\left\{\begin{array}{l}\frac{2}{n\pi}\left(\frac{y}{l}\cos\Omega t-\frac{x}{l}\sin\Omega t-\frac{ix}{l}\cos\Omega t-\frac{iy}{l}\sin\Omega t\right)\left(1-(-1)^n\right)\\ +\frac{2}{n\pi}(-1)^n(\cos\Omega t-\sin\Omega t)\end{array}\right\}e^{-\frac{n^2\pi^2}{d^2}vt}\\ -\frac{2\Omega\left(\Omega+\frac{ivn^2\pi^2}{d^2}\right)}{n\pi\left(\Omega^2+\frac{v^2n^4\pi^4}{d^4}\right)}\left(1-e^{-\frac{n^2\pi^2}{d^2}vt}\cos\Omega t+ie^{-\frac{n^2\pi^2}{d^2}vt}\sin\Omega t\right)\end{array}\right]\sin\frac{n\pi}{d}z. \tag{20}$$

Separating real and imaginary parts, we obtain

$$\frac{f}{\Omega l}=\frac{z}{d}+\sum_{n=1}^{\infty}\left[\begin{array}{l}\left\{\frac{2}{n\pi}\left(\frac{y}{l}\cos\Omega t-\frac{x}{l}\sin\Omega t\right)\left(1-(-1)^n\right)+\frac{2}{n\pi}(-1)^n(\cos\Omega t)\right\}e^{-\frac{n^2\pi^2}{d^2}vt}\\ -\frac{2\Omega^2}{n\pi\left(\Omega^2+\frac{v^2n^4\pi^4}{d^4}\right)}\left(1-e^{-\frac{n^2\pi^2}{d^2}vt}\cos\Omega t\right)+\frac{2vn\pi\Omega\sin\Omega t}{d^2\left(\Omega^2+\frac{v^2n^4\pi^4}{d^4}\right)}e^{-\frac{n^2\pi^2}{d^2}vt}\end{array}\right]\sin\frac{n\pi}{d}z, \tag{21}$$

$$\frac{g}{\Omega l}=\sum_{n=1}^{\infty}\left[\begin{array}{l}\left\{-\frac{2}{n\pi}\left(\frac{x}{l}\cos\Omega t+\frac{y}{l}\sin\Omega t\right)\left(1-(-1)^n\right)-\frac{2}{n\pi}(-1)^n(\sin\Omega t)\right\}e^{-\frac{n^2\pi^2}{d^2}vt}\\ -\frac{2\Omega^2\sin\Omega t}{n\pi\left(\Omega^2+\frac{v^2n^4\pi^4}{d^4}\right)}e^{-\frac{n^2\pi^2}{d^2}vt}-\frac{2vn\pi\Omega}{d^2\left(\Omega^2+\frac{v^2n^4\pi^4}{d^4}\right)}\left(1-e^{-\frac{n^2\pi^2}{d^2}vt}\cos\Omega t\right)\end{array}\right]\sin\frac{n\pi}{d}z. \tag{22}$$

To conclude, the unsteady flow of a viscous fluid caused by the rotations of two disks, which are initially at rest and impulsively start to rotate with angular velocity Ω has been investigated. The fluid is confined between two disks at $z = 0$ and $z = d$. The analytical solution of this problem has been presented. Thus, it has been shown that Pop's [3] problem can be addressed completely under the following two assumptions:

a. Changing initial conditions and keeping the fluid at infinity (presented by Erdogan [4]).

b. Keeping the boundary conditions same as Pop [3] and considering the flow between two disks (as presented in the present analysis).

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PARALLEL GENETIC ALGORITHMS FOR SIMULTANEOUS JOB SEQUENCING AND DUE DATE DETERMINATION – THE EARLINESS-LATENESS PROBLEM

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Abstract: The lean or just in time manufacturing philosophy makes not only the late completion of work undesirable but also the early completion of work since it results in the wastes of overproduction and unnecessary inventory. Hence, there is a need to solve the so-called earliness-lateness scheduling problem. The use of a pair of genetic algorithm's (GAs) running in parallel is introduced here to solve the earliness-tardiness job scheduling problem when the objective is a function of both the job sequence and the assignable due dates. One GA evolves a population of job sequences whilst the other simultaneously evolves a population of due dates. The best solution is then the job sequence and due date combination from the two populations that yields the best objective function value. The method is applied to good effect on example problems taken from the literature, once again demonstrating the relative ease with which a GA can be applied to different objective functions, unlike conventional mathematical programming or heuristic techniques that require considerable customization. A spreadsheet based, domain independent, general-purpose genetic algorithm (GA) approach is presented to solve the problem. Microsoft Excel™ and Evolver™ are used in this study.

***Keywords*:** Scheduling, genetic algorithm, earliness-tardiness

Introduction

The minimization of tardiness is a central objective in scheduling. Failure by industry to meet due dates results in financial penalties, loss of customer goodwill and a negative impact in a competitive environment. However, with the proliferation of the just-in-time or lean manufacturing philosophy, early completion is also highly undesirable, since it will result in a finished goods inventory with all its associated disadvantages such as the tying up of capital and storage space. The result is the need to solve the so-called earliness-lateness scheduling problem in which earliness as well as tardiness must be minimized. Reviews of the due date related scheduling problem are given in Baker and Scudder [1], Hall and Posner [2], Hall *et al.* [3] and Koulamas [4]. Most of the literature on scheduling, and the earliness-lateness problem in particular, assumes that due dates are specified *a priori*. However, in many instances the due dates for orders are negotiated rather than simply dictated by the customers. Therefore, there is a need to consider the due date as a decision variable, so that the due dates as well as the job sequences are varied in searching for an optimal schedule. This paper presents the design and application of parallel genetic algorithms (GAs) to seek optimal solutions to various objective functions formulated to penalize both earliness and tardiness.

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Why use genetic algorithms?

The application of genetic algorithms to scheduling has attracted much attention recently in the literature, with the following examples: Kim and

Kim [5]; Luu *et a*l. [6]; Ponnambalam *et al*. [7]; Ponnambalam *et al*. [8]; Onwubolu *et al*. [9].

Since the late 1980s there has been a growing interest in Genetic Algorithms (GAs) - stochastic optimization algorithms based on the principles of natural (Darwinian) evolution. They have been used widely for parameter optimization, classification and learning. Genetic algorithms (GA's) are directed random search algorithms based on the mechanics of natural selection and natural genetics. GA's are efficient search procedures that can identify optimal or near optimal solutions from solution populations. GA's operate as an iterative procedure on a fixed size of population of candidate solutions called chromosomes. In each iteration, the best solutions (chromosomes) are allowed to produce new solutions (children) by using the bits and pieces of each parent (by crossover) or by occasionally mutating features of a single parent. The worst members of the population die off to make way for the fitter individuals. The generic GA is illustrated in Figure 1.

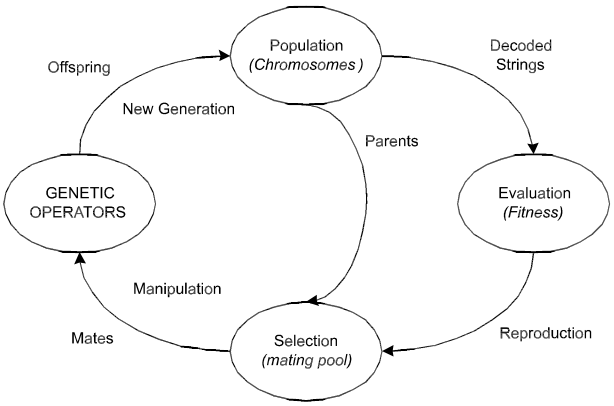

Figure 1. A Generic GA.

A typical genetic algorithm consists of the following steps:

a. ***Initialization:*** An initial population of solutions to the problem is generated, usually randomly. Each member of the population is called a chromosome. It is possible to 'seed' the initial population with some known 'good' solutions to speed up the algorithm but this can introduce a 'bias' into the solution.

b. ***Evaluation of the fitness function:*** The fitness value of each solution is calculated according to a fitness function (objective function), which measures the 'fitness' or 'goodness' of the solution.

c. ***Reproduction/Selection:*** Based on each individual's fitness a probabilistic selection mechanism chooses "mates" to act as parents in the genetic manipulation process. The selection policy is responsible for assuring survival of the fittest individuals. Eventually, this leads to the dominance of high-performing individuals in the population.

d. ***Genetic manipulation operations:*** New (child) chromosomes are generated from those selected for reproduction by applying genetic operators, principally crossover and mutation operators, to the parent chromosomes.

e. Steps ii, iii and iv are repeated until a stopping criterion is reached such as convergence of the best fitness value or a given number of iterations.

It is a characteristic of the schedule optimization process that once fairly good solutions have been formed their features will be carried forward into better solutions, and lead ultimately to optimal solutions. It is in the nature of a GA that new solutions are formed from the features of known good solutions. Therefore, it follows that GAs are particularly attractive for scheduling.

For simple n jobs and m machines schedule, the upper bound on the number of solutions is $(n!)^m$. Without n and m being very large this value soon becomes massive e.g. for 20 jobs and 5 machines the value is 8.52×10^{91}. Traditional approaches to schedule optimization such as mathematical programming and 'branch and bound' are computationally very slow in such a massive search

space. In contrast, GAs can traverse very large search spaces relatively rapidly and their mutation operator diverts the method away from local minima, which tend to become more common as the search space increases in size. Being suitable for large search spaces is an important advantage when dealing with schedules of increasing size since the solution space will grow very rapidly, especially when this is compounded by such features as alternative machines/routes. It is important that these large search spaces are traversed as rapidly as possible to enable the practical and useful implementation of automated schedule optimization. If the optimization is done quickly then production planners can try out 'what-if' scenarios and detailed sensitivity analysis as well as being able to react to 'crises' as soon as possible.

A practical advantage of GAs is that they provide a 'general purpose' solution to the scheduling problem, with the peculiarities of any particular example being accounted for in the fitness function and solution constraints without disturbing the logic of the standard optimization (GA) routine. This means that it is a relatively straightforward and simple matter to adapt the method to particular applications as they arise. This is in contrast to, for example, mathematical programming which can require much effort and mathematical skill when formulating the programming model.

The advantages of GAs are summarized by Gen and Cheng [10] as:

1. they do not have many mathematical requirements;
2. they search for solutions without regard to the specific inner workings of the problem;
3. they can handle any kind of objective function and any kind of constraints;
4. they can perform global search; and
5. they are flexible so can be hybridized with domain-dependent heuristics.

The sequence optimization GA

Detailed introductions to GAs are given by Goldberg [11] and Davis [12] and numerous more recent texts. For simultaneous sequencing and due date determination the use of two separate GAs in parallel is introduced, one for sequencing the jobs and another for due date determination – see figure 2. First, an initial population of randomly generated sequences of the tasks in the schedule is created by the first GA, whilst the other creates an initial population of due dates – encoded in binary as the number of days since 1st January 1900. These individual sequences and due dates are called 'chromosomes' and their fitness is calculated according to a user-defined fitness function such as: total makespan; mean tardiness; maximum tardiness; number of tardy jobs. The overall fitness of a sequence is recorded as the best fitness value achieved across the population of due dates. Similarly, the fitness of a given due date is the best fitness value achieved across the population of job sequences. This fitness evaluation is performed for each of the members of the initial populations and subsequent children produced by the GA. Each time a new job sequence is generated, the fitness of each of the existing due dates in the due date population is re-evaluated. Similarly, each time a new due date is generated, the fitness of each of the existing job sequences in the population of job sequences is re-evaluated. The overall best or fittest solution is the due date and job sequence combination giving the best objective function value. Three different objective functions involving due date determination are considered in this paper.

Once the initial populations have been formed, 'selection', 'crossover' and 'mutation' operations are performed repeatedly until the best fitness value converges i.e. very little improvement is observed over a given number of iterations. The 'selection' process consists of selecting a pair of parents from the current population using a rank-based mechanism to control the probability of selection. These parents then produce a child by applying a crossover

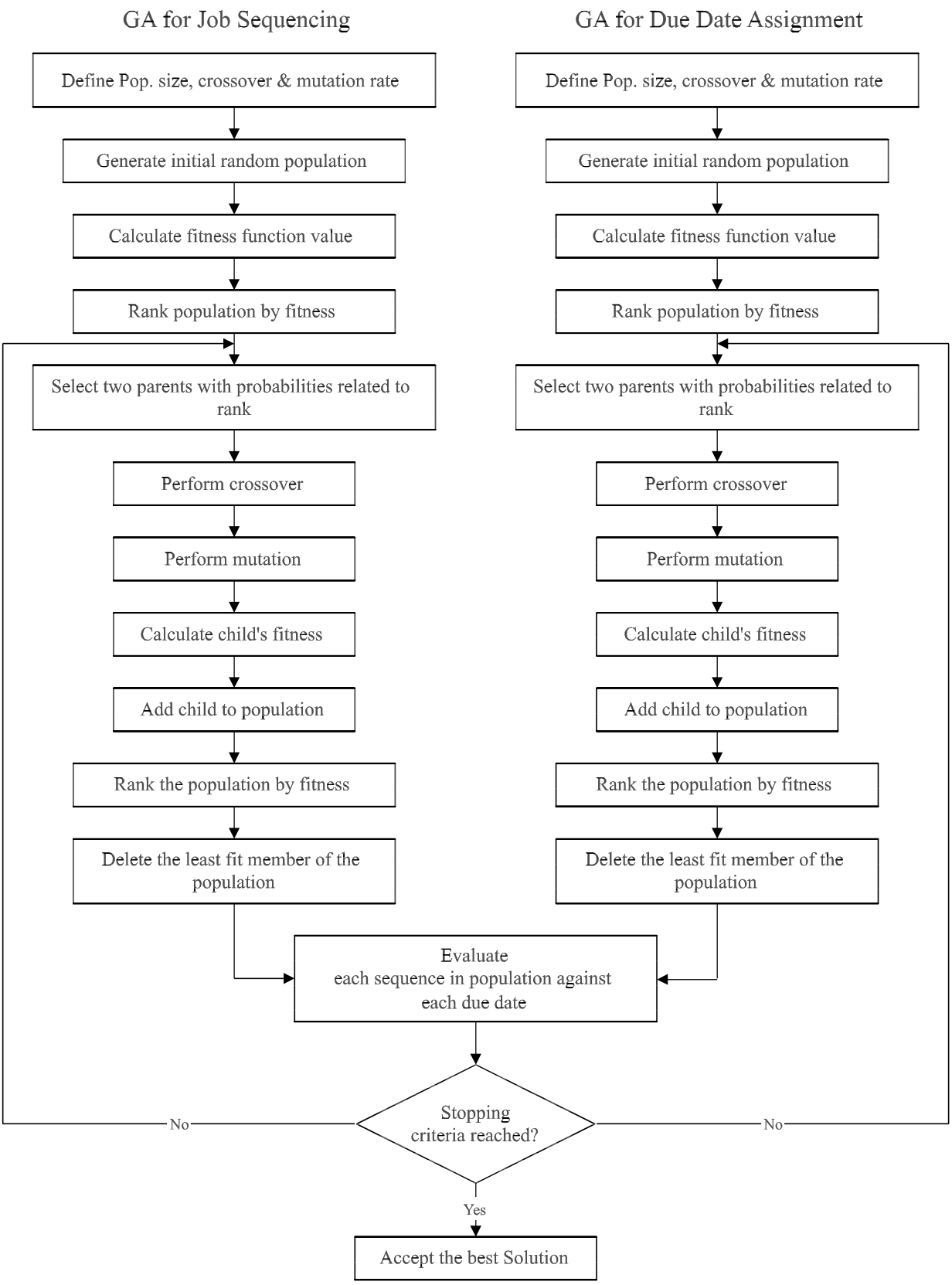

Figure 2. Flow chart of parallel Gas for Job Sequencing and Due Date Determination.

operator. The 'uniform order-based' crossover operator [12] is applied to the job sequences. This operator uses a randomly generated bit string (zero-one) template to determine for each parent which genes are carried forward into their child, as explained by the example in figure 3. Here, the template contains a one at positions {2, 3, 5, 6}. The genes (jobs) in these positions in parent-1 are carried straight across into the child. The template contains zeros at positions {1, 4, 7, 8}. In these positions parent-1 has genes {1, 4, 7, 8}. These genes are copied into the child in the same order as they appear in parent-2 {8, 4, 7, 1}. Uniform crossover is also applied to the due dates, but in a form suitable for binary numbers rather than sequences, as illustrated in figure 4, so that it does not require the final ordering step described in the previous sentence. The proportion of the genes coming from the first parent is defined by the crossover rate, which has a value between 0 and 1.

	Position in chromosome 1 2 3 4 5 6 7 8
Parent-1	1 2 3 4 5 6 7 8
Binary Template	**0 1 1 0 1 1 0 0**
Parent-2	8 6 4 2 7 5 3 1
Child	8 2 3 4 5 6 7 1

Figure 3. Job Sequence Chromosomes and the Crossover Operator.

	Decoded dd/mm/yy	Encoded - days since 1/1/1900, in binary 1 2 3 4 5 6 7 8 9 10
Parent-1	01/01/1901	0 1 0 1 1 0 1 1 1 1
Binary Template		**0 1 1 0 1 1 0 0 0 1**
Parent-2	01/01/1902	1 0 1 1 0 1 1 1 0 0
Child	26/05/1902	1 1 0 1 1 0 1 1 0 1

Figure 4. Encoded Due Dates and the Crossover Operator.

Following the crossover, the child may be mutated. For the job sequences, 'order-based' mutation is used. The probability that a job is mutated is defined by the mutation rate which lies in the range 0 to 1. Mutation consists of swapping the job with another job selected at random. To mutate the binary encoded due dates, a random number between 0 and 1 is generated for each bit. If this is less than the mutation rate (for example, 0.06), then the bit is mutated i.e. if it is a 0 it is set to 1 and vice versa.

Finally, the new child replaces the least fit schedule in the current population. In the experiments presented here population sizes of 50, crossover rates of 0.65 and mutation rates of 0.006 are used, and the GA stops when the change in the best objective function value in the last 100 iterations is less than 0.0001, i.e. very small.

Due date assignment with separate earliness and tardiness penalties

Dileepan [13] presents a branching algorithm to find the optimal schedule and common due date for a set of jobs, as given in Table 1.

Table 1. Job data for Dileepan's (1993) example.

Job	Process Time	Earliness Weight	Tardiness Weight
1	22	5	3
2	5	2	7
3	15	6	6
4	10	7	7
5	4	3	5

The objective function used by Dileepan contains separate earliness and tardiness penalties:

$$z = \sum_{d-C_i>0} b_i(d - C_i) + \sum_{C_i-d>0} a_i(C_i - d)$$

where:

C_i = completion date of job i;
d = the assigned due date;
b_i = earliness weight for job i;
a_i = tardiness weight for job i.

In this example the earliness and tardiness weights are assigned to jobs, in contrast to the next example where they are assigned to the position in the sequence. The aim is to find the job sequence and value for *d* for which *Z* is minimized. The best solution found by Dileepan is the job sequence 2-3-4-5-1, with common due date equal to 30 and *Z* = 208. The GA finds a different, although similar, job sequence 3-2-4-5-1, with the same value of Z. This highlights the GAs ability to find different solutions with the same Z value between different runs, due to the random aspects of the search mechanism.

Due date assignment with separate earliness, tardiness and due date penalties

Bector *et al*. [14] introduced the objective function:

$$\text{Minimize } Z = \sum_{i=1}^{n} (wk + w_{ij} E_i + w_{ij} T_i)$$

where

n = *total number of jobs;*
w = the due date assignment cost per unit time;
k = common due date associated with a sequence;
w_{ij} = positional weight of job *i* in position *j* - each position in the schedule has a weight so that a job is assigned the weight for the position it is in;
E_i = the earliness of job i;
T_i = the tardiness of job i.

They use the linear goal programming approach to determine the optimal job sequence and due date combination, as applied to the data in Table 2.

Table 2. Job data for Bector et al's (1991) example.

Job	Process Time	Positional Weight
1	3	3
2	4	2
3	6	5
4	9	4
5	14	3
6	18	6
7	20	2

They find the minimum objective function value of *Z*=244 with the job sequence 7-5-4-2-1-3-6 and a common due date of 47. This solution is indeed optimal and the GA finds the same solution.

Panwalker *et al*. [15] also address this type of problem, but instead of positional weights they use different penalties for job earliness and tardiness. Their objective function is:

$$\text{Minimize } Z = \sum_{i=1}^{n} (P_1 d + P_2 E_i + P_3 T_i)$$

where:

P_1 = due date assignment cost per unit time;
P_2 = earliness cost per unit time;
P_3 = tardiness cost per unit time;
E_i = earliness of job i;
T_i = tardiness of job i.

Their example data are given in Table 3.

Table 3. Job data for Panwalkar *et al's* (1982) example.

Job	*Process Time*
1	3
2	4
3	6
4	9
5	14
6	18
7	20

The weights P_1, P_2 and P_3 are 5, 11 and 18 respectively. Panwalkar *et al*. develop a heuristic algorithm to solve this problem. They find the minimum objective function value of Z=2664 with a job sequence 6-4-2-1-3-5-7 and a common due date of 34. This solution is indeed optimal and the GA finds the same solution.

Due date assignment to minimise sum of absolute deviation from due date

Bector *et al*. [16] minimize the sum of the absolute deviations from a common due date. They develop an algorithm based on linear goal programming which determines an optimal due date and the corresponding optimal sequence of jobs. The objective function is:

Minimize $z = \sum_{i=1}^{n} |d_i|$

where:

d_i = deviation of finish time of job i from due date.

The data for their example is given in Table 4.

Table 4. Job data for Bector et al's (1988) example.

Job	*Process Time*
1	9
2	14
3	6
4	3
5	4
6	20
7	18

The minimum objective function value found by Bector *et al*. is Z=83 with a job sequence of 6-2-3-4-5-1-7 and a common due date of 43. The GA finds the same minimum objective function value but with a job sequence of 6-7-1-5-4-3-2 and a common due date of 51. At first sight it might appear that the solution of Bector ***et al*** is better because the due date is earlier. However, this is not necessarily the case since it could mean an excessive build-up in the finished-goods inventory; no consideration is given to the inventory produced by each job. The objective function is the objective and the solutions are equally good in this respect. Once again, repeated runs of the GA can find different solutions – including the one found by Bector *et al*.

In the present study, the application of two parallel GAs has been introduced for the optimization of job scheduling objectives which are functions of both the assignable due dates and the job sequence, so that both must be varied in the search for the best job sequence/due date combination. This principle of parallel GAs can be carried forward into other, similar multi-variable objective functions. The application presented also demonstrates the relative ease with which a GA can be applied to different objective functions, unlike conventional mathematical programming or heuristic techniques that require considerable customization for different objective functions.

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TRENDS IN CAPACITY REALIZATION IN BANGLADESH MANUFACTURING SECTOR

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Abstract: The paper studies to examine the question of capacity realization rates of manufacturing industries of Bangladesh using the following three measures of capacity realization- Wharton measure, Minimum capital output ratio measure and Single time trend measure. Twenty-three industry groups in Census of Manufacturing industries (CMI) reports have been classified into four use-based sectors. The range of variation in capacity realization is between 50 to 153 percent for twenty-three industry groups. Single time trend measure indicate high realization rates and other measures namely, Wharton and Minimum capital output ratio measure reveal close correspondence both in their levels and in their movement. There is evidence to suggest a decline in the capacity realization over the period. The trends in capacity realization index by alternative methods are also examined.

***Keywords*:** Capacity realization, maximum potential output, capital stock

Introduction

An understanding of the forces that influence capacity realization is essential for successful industrial policy formulation and providing guidance for planned sectoral investment allocations. Especially the less developed countries, where capital is scarce (such as Bangladesh), can ill afford under-realization in their production capacities. Productive capacity realization is an important aspect of production performance that has received little attention in measuring the productivity growth of economic agents. The reason for this is that traditional theory of firm assumed away capacity under realization, or any form of inefficiency in production. Measurement of capacity realization becomes important in analyzing the impact of policy changes on the productivity performance of firms. Measures of industrial capacity realization (hereafter, CR) have been used extensively in helping to explore changes in the rate of investment, labor productivity and inflation. The CR measures have also been used to obtain indices of capital in use, as distinct from capital stock in place. Winston [18], Hogan [8], Kemal and Allauddin [10] had shown that rates of capacity realization were generally low, particularly if capacity is measured in terms of multi-shift operation. Hogan had taken capacity on a three-shift basis and found realization to be around 25 percent only in Pakistan while the corresponding estimates of Winston [18] and Kemal and Allauddin [10] were 40 percent and 50 percent respectively. In India, during the formulation of the Second five-year plan, Vakil [17] focused attention on this problem. In one study, Sastry [16] has made an attempt to analyze comparative empirical evaluation for cotton mill industry in India. Goldar and Renganathan [5] argued that differential performance of firms in terms of realization of productive capacity can be analyzed through the well-known structure conduct performance theory of industrial economics. Porter [15], Oster [14] and Caves and Barton [4] also maintained that inter-industry differences in efficiency and capacity realization result from inter-industry differences in stable elements of market structure.

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Using industry level data for 1973/74, Afroz and Roy [2] found that capacity realization varied from 22 percent to 75 percent in selected manufacturing industries. While using enterprise level survey data for 1970, Habibullah [6] found that the efficiency of the best-performed firm was seven times higher than that of the worst performed firm. Abdullah and Rahman [1] showed that the rate of capacity realization in textile industries in Bangladesh has been low, ranged from an average rate of 30 percent to 52 percent from 1963 to 1982. Using a similar method and enterprise level survey data for 1992, the most recent study of Bhattachayra [3] found average rates of capacity realization of 69 percent for cotton textiles, 65 percent for garment industry and 71 percent for food processing industry.

Some earlier studies found substantial variations in capacity realization across firms and industries in the Bangladesh manufacturing sector. Various approaches have been attempted in the past in the measurement of capacity realization. As no single measure appears entirely satisfactory in Bangladesh, it may be both necessary and desirable to consider alternative measures and evaluate them before forming a judgement about the extent of capacity realization. No attempt seems to have been made so far at such comparative empirical evaluation for Bangladesh Manufacturing Industry. The present study is a modest attempt in this direction. The main purpose of this study is to capture the efficiency aspect of the manufacturing enterprise. Capacity realization provides insight into the performance of manufacturing enterprise and also aids in identifying factors, which influence industrial growth. The focus is mainly on the question of capacity realization rates, trends in capacity realization following Wharton measure as well as minimum capital ratio measure and single trend measure. In this paper, construction and measures of the capacity realization along with the sources of data is described first followed sequentially by a critical appraisal of alternative measures of capacity realization, the results and discussion of estimates of capacity realization by alternative measures and finally the policy implications of the study.

Materials and Methods

Data and Estimation Procedure

The annual reports of Census of manufacturing industries (CMI) published by Bangladesh Bureau of Statistics are classified into the following sectors. The industries, which feature in these sectors are listed below in the aggregation scheme.

Consumer non-durables: (i) Food manufacturing, (ii) Beverage industries, tobacco manufacturing, (iii) Textile manufacturing (iv) Mfg. of wearing apparels, (v) Leather and its products, and (vi) Paper and its products.

Intermediates: (i) Manufacturing of rubber products, (ii) Manufacturing of plastic products, (iii) Petroleum refining, (iv) Misc. petroleum products, (v) Industrial chemicals, (vi) Other chemical products, (vii) Non-metal minerals products, and (viii) Iron and steel basic industries.

*Consumer durables***:** (i) Wood and wood products, (ii) Furniture manufacturing, (iii) Structural metal products, (iv) Fabricated metal products, and (iv) Other manufacturing industries.

Capital goods: (i) Non-electrical machinery, (ii) Electrical machinery, and (iii) Transport equipment manufacturing.

Time series data on gross fixed capital formulation and value of output is compiled from CMI for the period 1981-82 to 1991-92 for the four industrial sectors under study. No CMI report is available after this period. These variables are converted to real values in the following way:

Capital (K): Capital is one of the essential inputs in measuring productivity. Gross fixed assets are used in this study as capital inputs. It includes

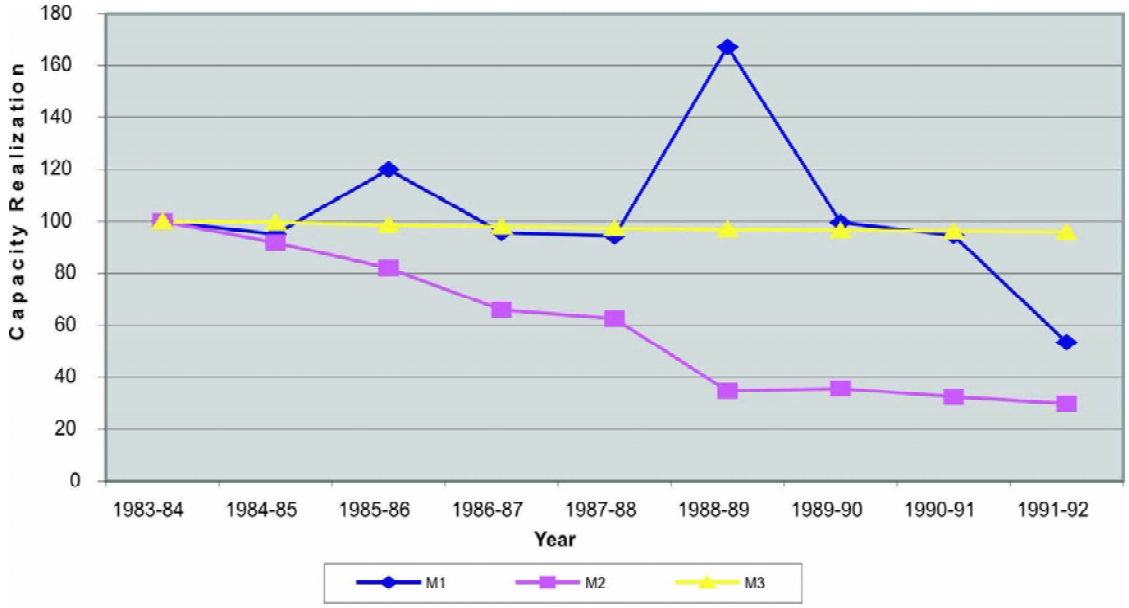

Figure 1. Consumer non-durable industries Alternative Measures of Capacity Realization.

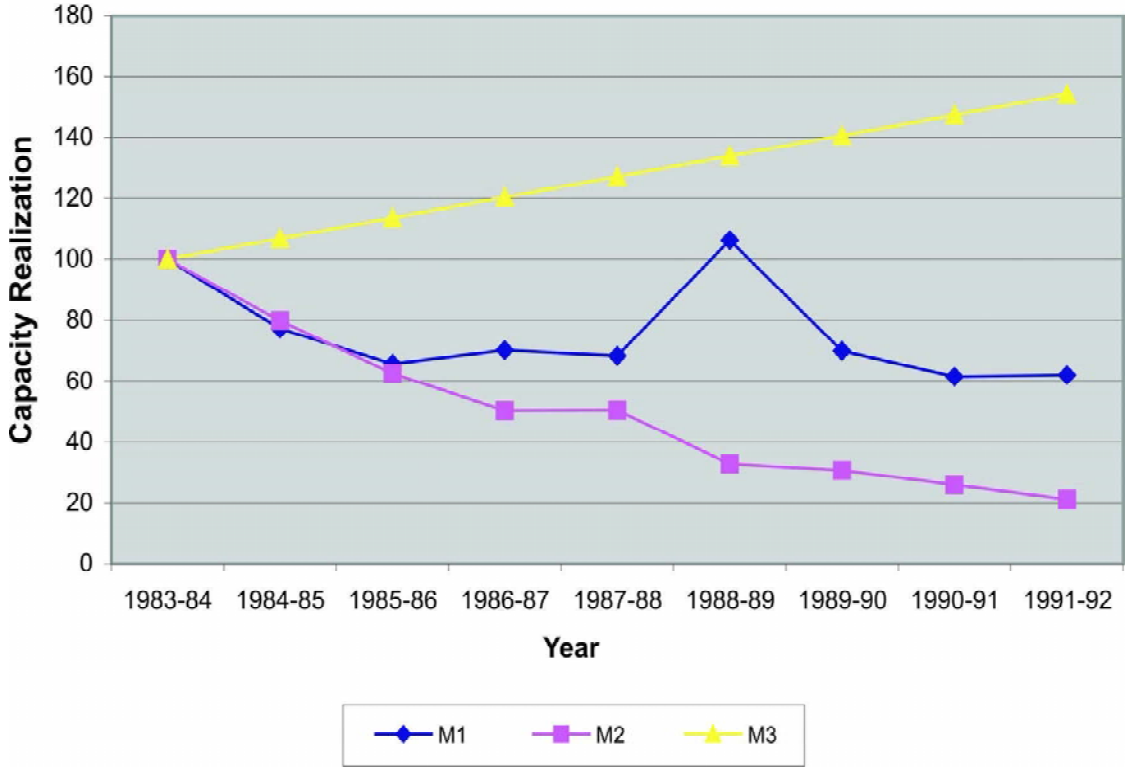

Figure 2. Intermediate durable Industries Alternative Measures of Capacity Realization.

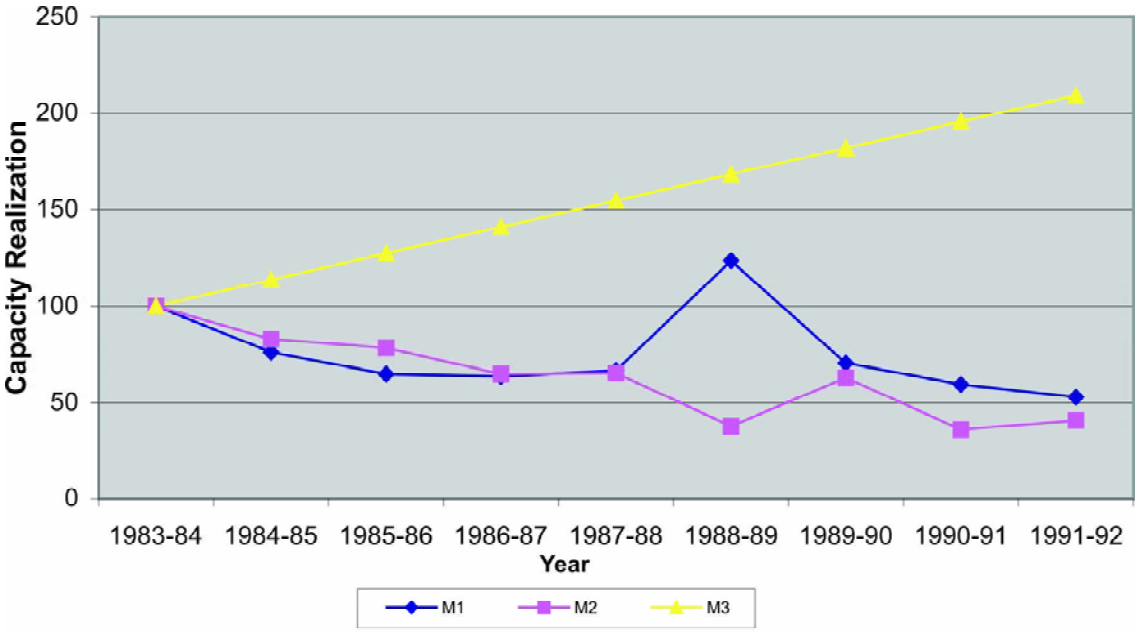

Figure 3. Consumer Durable Industries Alternative Measures of Capacity Realization.

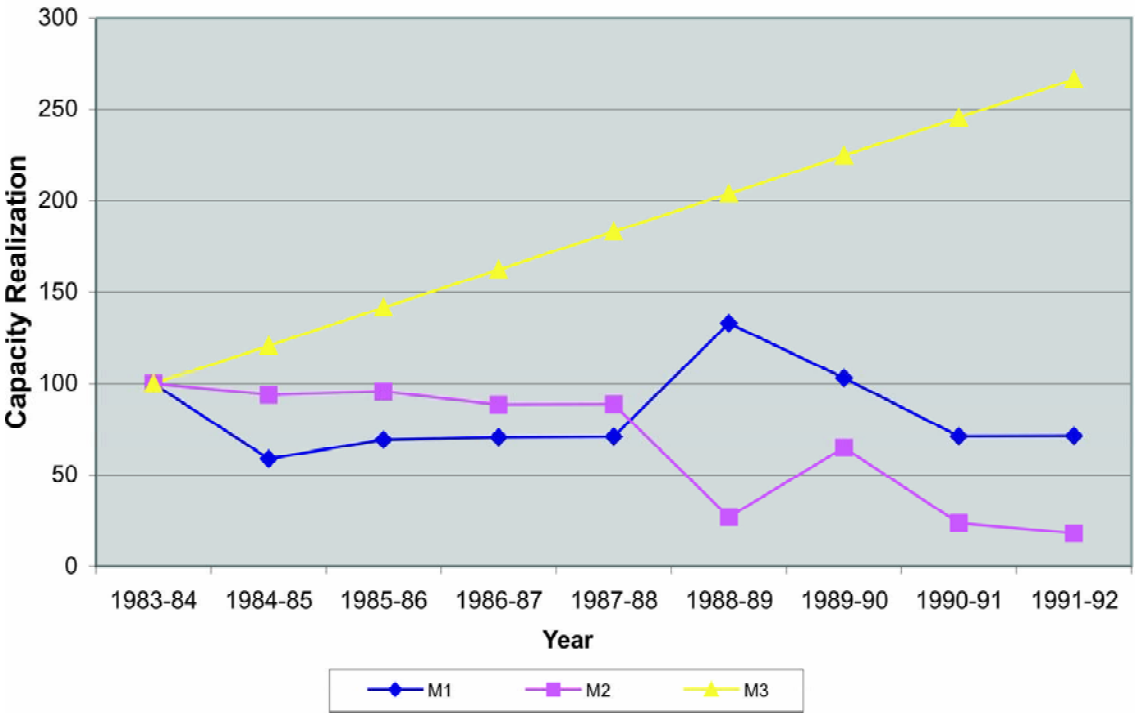

Figure 4. Capital Goods Industries Alternative Measures of Capacity Realization.

the book values of land, buildings, machinery, tools, transport and office equipment, etc. The gross value of fixed assets has been weighted by the base year rate of return to get a measure of capital input. The rate of return is the ratio of non-wage value added to fixed assets as used here. And then the weighted capital input was deflated by the capital goods price index that stands as wholesale machinery price index.

Value added (V): Gross value added figures are used in this study to represent value addition which is equal to gross output minus industrial cost. Industrial costs include cost of raw materials, fuel and electricity. We use value added instead of net value added to avoid the arbitrariness involved in depreciation estimates. To obtain the gross value-added series in 'constant prices', the yearly current values were deflated by the Industry price index of the relevant year.

Capacity realization index by minimum capital-output ratio measure is obtained in the following manner.

Capacity realization index by this measure requires calculation of real capital output ratios for the four industrial sectors. We find out the benchmark years for the four sectors where the real capital-output ratios are minimum. The benchmark years for the four sectors are obtained by dividing the real fixed capital by the minimum capital-output ratio. Finally the index is obtained by dividing the real value of output by estimate of capacity.

Capacity realization using Wharton measure or the trend through peaks method is computed for each sector by dividing the current year's real value of output by previous peak output. For any given year, the preceding year's output is scanned and the maximum among them is selected as the peak output. This procedure is implemented for every successive year. The capacity realization index using single time trend measure is also similarly obtained.

Merits and demerits of methods

The Wharton index of Capacity Realization

The simplest in the class of conventional approach is Wharton's 'trend-through-peak' method. This method is based on output series data. The basic principle underlying this approach is that capacity grows at a constant absolute amount for several periods, switches to growth by a different constant amount for another set of periods, and so on, so that ' trend-through-peak's of actual output indicate the full capacity output. Therefore, fitting a straight line through the successive peaks of actual output by linear interpolation produces capacity output. So the Productive Capacity realization (PCR) index of any time is $W_t = V_t / V_t^W$ where W_t is Wharton index of realization rates, V_t is actual output and V_t^w is capacity output taken from Wharton trend output. This method has been widely used in earlier studies (Klein and Summer [11], McMohan and Smyth [12], O'Relly and Nolan [13], Sastry [16] and Harris and Taylor [7]. However, the method has been criticized for several reasons. First, selection of series-monthly, quarterly or yearly series is difficult as is identification of peaks and piece-wise linearisation. Second, it does not take into account the growth of inputs in estimating capacity output.

The Productivity of Capital Method

This method is a modified version of the Wharton index. Since output is constrained by stock of plant and machinery, estimates of capacity output can be obtained by fitting a straight line through the peaks of the output-capital ratio and then realization rates can be estimated by the following: $MW = V/K \big/ (V/K)^*$, where MW is a modified wharton index, V/K ratio of output to capital and $(V/K)^*$ estimated full capacity levels of V/K, obtained by interpolating between selected peak

levels of V/K. The advantage of this method is that, unlike the Wharton method, capacity output is subject to capital constraint. However, the disadvantages are many, most importantly, its ignorance of non-capital inputs and its inability to allow for factor substitution.

Minimum Capital-Output ratio Method

In this method, capital-output ratios are estimated with constant prices. A benchmark year is chosen, on the basis of a low capital output ratio, and considered as the capacity output. The estimate of capacity is obtained from real fixed capital stock, deflated by the minimum capital-output ratio, and realization rates are then obtained using the following formula: $PCR = V/\hat{K}$ where $\hat{K} = \frac{K}{(K/V)_{\min}}$, PCR= Productive Capacity Realization, V= Real output (Gross value added), $\hat{K}$ = Estimated capacity, K= Real fixed capital and $(K/V)_{\min}$ = Minimum of capital-output ratio. This is a useful alternative measure of capacity realization. However, the usefulness of this approach depends on the accuracy of the measurement of capital.

Single Time Trend Method

This method involves regressing actual output over a time variable, i.e, $V = a + bt$ and using this estimated output as capacity output, obtaining the realization rates in the usual manner. This method is very simple and takes account of endogenous factors that affect the realization index. However, capacity output is underestimated and hence realization rates are overestimated, since capacity outputs are taken from the regression, which provides only average performance over the year.

Of these above mentioned measures, the Wharton index has been popularly used . There are two other measures of capacity realization, viz, the Shift measure and the Electricity Consumption (U_E) Measure. In the shift measure, the actual number of shifts worked in a year is compared with the available number of shifts, on the assumption that a certain numbers of shifts can be operated daily. The electricity consumption is used as an indicator of capital usage developed by Jorgenson and Grilliches [9]. Electricity consumption is fairly a good indicator of capacity realization.

Results and Discussion

We used the published data on production and capacity realization in the Bangladesh industries to analyze the variations in the realization levels across industries. Several characteristics of time series of capacity realization may be examined in this context. These are peaks and troughs, absolute levels, period average, coefficient of variation and the overall trend. We notice that the capacity realization indices obtained through Wharton measure, Minimum Capital-Output ratio measure and Single time trend method follow correspondence for four of the industrial groups. These groups are Consumer non-durable, Intermediates, Consumer durable and Capital goods.

A comparison of the various alternative measures of capacity realization reveals several points of interest in Table 1. First of all, the range of variation in capacity realization is rather wide. The capacity realization ratios for capital goods have been consistently higher than those of consumer non-durable industries, intermediate industries and consumer durable industries. For consumer non-durable industries, the capacity realization rate obtained from Wharton measure varies between 53% and 167%, which is larger than that for other industrial groups. For consumer durable industries, the capacity realization rate varies from 52% to 123% and for intermediates and capital goods the rates vary between 61% and 106% and 59% and 133%, respectively. The capacity realization series obtained by the minimum capital-output ratio measure is found to possess an opposite direction of trend as compared to the same series obtained by the other

Table 1a. Capacity realization by alternative measures in Bangladesh industries. Method 1: Capacity realization index based on Wharton measure, Method 2: Capacity realization index based on minimum capital output ratio measure and Method 3: Capacity realization index based on single time trend measure.

Year	Consumer non-durable industries			Intermediate durable industries		
	Method 1	Method 2	Method 3	Method 1	Method 2	Method 3
1983-84	100.00	100.00	100.00	100.00	100.00	100.00
1984-85	94.98	91.74	99.59	77.24	79.84	106.78
1985-86	119.91	81.97	98.56	65.62	62.51	113.56
1986-87	95.58	65.91	97.92	70.23	50.28	120.35
1987-88	94.26	62.47	97.36	68.36	50.42	127.13
1988-89	167.20	34.72	96.89	106.35	32.77	133.91
1989-90	99.60	35.46	96.48	69.97	30.72	140.69
1990-91	94.55	32.27	96.12	61.52	25.89	147.47
1991-92	53.45	29.74	95.79	62.02	21.12	154.26
Mean	102.17	59.36	97.63	75.70	50.39	127.13
S.D.	25.934	1.41	15.415	25.01	17.509	21.177
C.V.	27.576	43.69	1.449	20.363	49.629	13.773

Table 1b. Realization by alternative measures in Bangladesh industries.

Year	Consumer non-durable industries			Intermediate durable industries		
	Method 1	Method 2	Method 3	Method 1	Method 2	Method 3
1983-84	100.00	100.00	100.00	100.00	100.00	100.00
1984-85	76.11	82.83	113.67	59.07	93.96	120.80
1985-86	64.73	78.28	127.34	69.33	95.67	141.60
1986-87	63.52	64.70	141.01	70.74	88.44	162.39
1987-88	66.64	65.10	154.68	71.16	88.74	183.19
1988-89	123.37	37.65	168.35	133.09	27.23	203.99
1989-90	70.40	62.79	182.02	103.20	65.07	224.79
1990-91	59.28	36.02	195.69	71.22	23.77	245.58
1991-92	52.74	40.62	209.36	71.53	18.16	266.38
Mean	75.198	63.11	154.68	83.26	66.782	183.191
S.D.	21.177	20.748	35.295	22.424	32.333	53.698
C.V.	28.162	32.876	22.818	26.933	48.415	29.312

two methods. The capacity realization series obtained by Single time trend method reveals upward trends for the three industrial groups with the exception of consumer non-durable. Single time trend measures of capacity realization indicate that the mean levels of capacity realization during the period were more than 95% for all industrial groups. The intermediates and consumer durable industry groups display a lower mean level of capacity realization (75%), whenever we estimate capacity realization by Wharton measure.

Table 2 reveals how well our capacity realization indices for the various industrial groups perform vis-a-vis real output series for the same sector. For the consumer non-durable industries, the degree of association is more than 45% between output series and capacity realization series obtained by the Wharton method. On the other hand, the correlation coefficient taken between output series and capacity realization series obtained by minimum capital-output ratio and single time trend methods indicates opposite direction of association. But the correlation coefficients obtained by minimum capital-output ratio measure, is significant at the 0.05 level. The low values of correlation coefficients between

Table 2a. Correlation coefficients between output and capacity realization series. VAD for output index . M1 for Capacity realization index based on Wharton measure, M2 for Capacity realization index on minimum capital output ratio measure andM3 for Capacity realization index based on single time trend measure.

Consumer non-durable Industries

		VADCOSND	CONNDM1	CONNDM2	CONNDM3
Pearson Correlation	VADCOSND	1.000	.460	-.747*	-.648
	CONNDM1	.460	1.000	.018	.149
	CONNDM2	-.747	.018	1.000	.978
	CONNDM3	-.648	.149	.978	1.000

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).

Intermediate goods Industries

		VADINTER	INTERM1	INTERM2	INTERM3
Pearson Correlation	VADINTER	1.000	.306	-.632	636
	INTERM1	.306	1.000	.418	-.431
	INTERM2	-.632	.418	1.000	-.961
	INTERM3	.636	-.431	-.961	1.000

** Correlation is significant at the 0.01 level (2-tailed).

Table 2b. Correlation coefficients between output and capacity realization series.

Consumer Durable Industries

		VADCOSD	CONDM1	CONDM2	CONDM3
Pearson Correlation	VADCOSD	1.000	.235	-.713	.732
	CONDM1	.235	1.000	.114	-.342
	CONDM2	-.713	.114	1.000	-.904
	CONDM3	.732	-.342	-.904	1.000

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).

Capital goods Industries

		VADCAPIG	CAPIM1	CAPIM2	CAPIM3
Pearson Correlation	VADCAPIG	1.000	.358	-.842	.877
	CAPIM1	.358	1.000	-.300	101
	CAPIM2	-.842	-.300	1.000	-.879
	CAPIM3	.877	.101	-.879	1.000

** Correlation is significant at the 0.01 level (2-tailed).

capacity realization series obtained by Wharton measure and the degree of association is more than 95% obtained by minimum capital-output ratio measure that is also significant at the 0.01 level. The value of correlation coefficient indicates that the output series and capacity realization series obtained by single time trend measure bear close resemblance to the remaining three industry groups. On the other hand, the output series and capacity realization series obtained by Wharton measure bears close resemblance in all the industry groups. The correlation coefficient between the output series and capacity series based on minimum capital output ratio measure takes the value to opposite sign but is significant at the either 0.01 or 0.05 level for almost all industrial groups. The low value and opposite sign of correlation coefficients between capacity realization series obtained by single time trend measure and suggest that one has to reject the capacity realization series of this method. On the other hand, the opposite sign of correlation coefficients between capacity realization series based on minimum capital-output ratio and single time trend measure are significant at either 0.01 or 0.05 level for all industrial groups.

In conclusion, capacity realization has been measured in four industrial groups in an attempt to explain capacity realization based on alternative measures. A comparison of the results by obtained following application of these alternative measures in capacity realization suggests the following. The estimates of capacity realization vary according to the measure employed. The range of variation is between 50 to 183 percent. However, Single time trend measure indicate high realization rates and other measures, namely, Wharton and Minimum capital output ratio measure reveal close correspondence both in their levels and in their movement. There is evidence to suggest a decline in the capacity realization over the period. The analysis also shows that one has to reject the capacity realization series on minimum capital output ratio measure. The study shows that there is considerable under-realization of capacity in various industries of Bangladesh. The situation is not likely to improve unless serious attempt is made to remove the basic causes identified such as the low-paucity of foreign exchange, limited market demand for the product, imbalance of machinery, skilled labor deficiency and managerial difficulties, failure in power supply, mechanical/ maintenance trouble, and strike/gheraos.

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Note

INTEGRAL RELATIONSHIP BETWEEN HERMITE AND LAGUERRE POLYNOMIALS: ITS APPLICATION IN QUANTUM MECHANICS

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The associated Laguerre polynomials can be represented by a certain integral over the Hermite polynomials. This fact allows determining, in a simple way, the matrix elements of the one-dimensional harmonic oscillator, and also the radial wave function for the Morse potential. In fact, a well-known representation for Laguerre polynomials for z > 0, m ≥ n exists [1 – 3]:

$$L_n^{m-n}(-z) = \frac{(-1)^{m-n}}{(2z)^{\frac{m-n}{2}}\, 2^n n!\sqrt{\pi}} \int_{-\infty}^{\infty} e^{-\left(x+\sqrt{\frac{z}{2}}\right)^2} H_m(x) H_n(x)\, dx \qquad (1)$$

where H_n and L_n^k are the Hermite and associated Laguerre polynomials [4], respectively. We show that (1) gives us a simple manner to determine matrix elements of the one-dimensional harmonic oscillator (HO) in quantum mechanics:

$$f(\beta) \equiv \left\langle m \left| e^{-\beta x} \right| n \right\rangle = \int_{-\infty}^{\infty} \Psi_m^*(x) e^{-\beta x} \Psi_n(x)\, dx \ , \quad (2)$$

being $\beta \geq 0$ an arbitrary parameter. Besides, we find that $f(\beta)$ satisfies a differential equation which permits us to obtain the radial wave function for the Morse potential [5-10].

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The normalized wave functions for HO in natural units (i.e., $\hbar = 1$, m (mass)=1, w (angular frequency)=1) are given by:

$$\Psi_n(x) = \frac{1}{\left(n! 2^n \sqrt{\pi}\right)^{1/2}} e^{-\frac{x^2}{2}} H_n(x) \ , \ n = 0,1,2,..., \quad (3)$$

Using (1) and (3), (2) becomes:

$$f(\beta) = \sqrt{\frac{n!}{m!}} \left(-\frac{\beta}{\sqrt{2}} \right)^{m-n} e^{\frac{\beta^2}{4}} L_n^{m-n}\left(-\frac{\beta^2}{2} \right), \quad (4)$$

in accordance with several expressions reported in the literature [11-14].

It is interesting to note that (4) and the associated Laguerre differential equation [4] imply that $f(\beta)$ satisfies the equation:

$$\beta^2 \frac{d^2 f}{d\beta^2} + \beta \frac{df}{d\beta} - \left(\frac{\beta^4}{4} + A\beta^2 + Q \right) f = 0 \quad (5)$$

where $A = m + n + 1$ and $Q = (m-n)^2$; that is, (4) is a solution of (5). We shall employ $f(\beta)$ to resolve the radial Schrödinger equation for the Morse interaction.

Morse [5-10] introduced the potential:

$$V(r) = D[e^{-2a(r-r_0)} - 2e^{-a(r-r_0)}] \qquad (6)$$

as an approximation to vibrational motion of a diatomic molecule, where D is the dissociation energy (well depth), r_0 is the nuclear separation and a is a parameter associated with the well width, such that $\frac{a}{2\pi}\sqrt{2D}$ gives the frequency of small classical vibrations around r_0. Change of variable $u = r - r_0$ and use of natural units, then gives the Schrödinger equation:

$$\frac{d^2}{du^2}\Psi_M + 2\left[E - D\left(e^{-2au} - 2e^{-au}\right)\right]\Psi_M = 0 \ , \qquad (7)$$

with $\frac{1}{r}\Psi_M$ as the Morse's radial wave function.

If now we employ another independent variable β in (7) defined by:

$$\beta = i\sqrt{2k}e^{-\frac{au}{2}} \ , \ k = \frac{2}{a}\sqrt{2D} \ , \ i = \sqrt{-1} \qquad (8)$$

then (7) adopts the form:

$$\beta^2\frac{d^2}{d\beta^2}\Psi_M + \beta\frac{d}{d\beta}\Psi_M - \left(\frac{\beta^4}{4} + k\beta^2 - \frac{8E}{a^2}\right)\Psi_M = 0 \qquad (9)$$

with the same structure as (5). Then, by a formal comparison of (5) with (9) we deduce that:

$$k = m + n + 1 \ ,$$
$$E_n = -\frac{a^2}{8}(m-n)^2 = -\frac{a^2}{8}(k-2n-1)^2 \qquad (10)$$

which implies that it is not possible to have $m = n$, because otherwise the value $E = 0$ is forbidden for bound states. Thus from (10) it results that $k > 1$, which is the condition [5] for the existence of a discrete energy spectrum. Besides, as $E_n \neq 0$ and $k > 1$, then (10) leads to $(k - 2n - 1) > 0$, that is, $0 \leq 2n < (k-1)$ which means [7] a finite number of bound states.

From (5) and (9) it is clear that Ψ_M is proportional to $f(\beta)$ given by (4), then:

$$\Psi_M(r) = \sqrt{\frac{abn!}{\Gamma(k-n)}}q^{\frac{b}{2}}e^{-\frac{q}{2}}L_n^b(q) \qquad (11)$$

where $q = ke^{-a(r-r_0)}$ and $b = m - n = k - 2n - 1$, in accordance with [15] for $\frac{1}{r}\Psi_M$ normalized to unity.

Thus, we see that the Schrödinger equation is easily resolved for the vibrational Morse oscillator, using the matrix elements $\left\langle m\left|e^{-\beta x}\right|n\right\rangle$ for the one-dimensional HO. This is another example of relationship [8,16,17] between the Morse and harmonic oscillators.

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