

DEVELOPMENT AND VALIDATION OF UV SPECTROSCOPIC AND HPTLC METHODS FOR SIMULTANEOUS ESTIMATION OF DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE AND PIOGLITAZONE HCL IN SYNTHETIC MIXTURE

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Abstract : In the present study uv spectroscopy and HPLC methods were developed and validated for the simultaneous analysis of dapagliflozin propanediol monohydrate and pioglitazone Hcl in a synthetic mixture. Uv spectroscopy was developed using first order derivative spectroscopy method. The zero crossing point (ZCP) was obtained at 216.20nm and 221.80nm for the estimation of DAPA and PIO respectively, HPTLC method is an advanced and modern analytical technique based on the principle of thin layer chromatography, which provides essential benefits, such as improved sample application, better and faster separation, and less mobile phase usage. The methods were validated in terms of linearity, accuracy(%recovery), precision (Interday, intraday, and reproducibility), and robustness. Both the methods were linear ($R^2=0.993-0.999$) and accurate (%recovery was 98.45% - 101.93% for the UV method and 98.26% - 102% for the HPTLC method) The method was also found precise (%RSD<2%) and robust. Any one of the validated methods can be used for the analysis of dapagliflozin propanediol monohydrate and pioglitazone Hcl in a synthetic mixture. so, the method was found to be accurate, precise, specific, selective, repeatable, robust, and reproducible.

Keywords:- - Dapagliflozin propanediol monohydrate, Pioglitazone hydrochloride, UV spectroscopy, , HPTLC,

INTRODUCTION

Hospital or health care waste is generally named & popular as biomedical waste. The world health organization defines biomedical waste as ,”Waste generation by health care activities & includes blood, used needles, pharmaceuticals, radioactive materials etc.” The biomedical waste is also known as infectious waste or medical waste or health care waste. According to biomedical waste management & handling rules 1998 of India. Biomedical waste means any waste which is generated during the diagnosis, treatment or immunization of human being or animals or in research activities. In simple words biomedical waste is the waste generated by the medical & health institute/agencies.

Biomedical waste management defines waste management as the practices & procedures or the administration of activities that provide for the collection, source separation, storage, transportation, transfer, processing, treatment & disposal of waste . Biomedical waste management is a routine procedure of hospital administration as prescribed by law .Hospital waste , hospital acquired infection , transfusion transmitted diseases, rising incidence of hepatitis B, HIV & Other diseases, create potential threat of infection, contamination & serious health hazards to doctors, nurses, ward boys, support staff, sanitation workers, rag pickers & other health care workers. Who are regularly exposed to biomedical waste as an occupation hazards as well as general public in the surrounding area .

NEED OF THE STUDY.

The establishment of large hospitals where hundreds to thousands of patients are treated , it has created a serious problems of biomedical waste management. The seriousness of improper biomedical waste management was brought to the light during summer 1998. In India studies have been carried out at local / regional levels in various hospitals, indicate that roughly about 1-5 kg/bed/day to waste is generated. Among all health care personnel ,ward boys , sweepers, operation theatre & laboratory attendants have come into contact with biomedical waste during the process of segregation , collection, transport, storage & final disposal . The knowledge of medical , paramedical staff & ward boys , sweepers about the biomedical waste management is important to improve the biomedical waste management practices. The biomedical waste requiring special attention includes those that are potentially infectious , sharps ,example needle , scalpels , objects capable of puncturing the skin , also plastic ,pharmaceutical & chemically hazardous substances used in laboratories etc.

3.1Population and Sample

KSE-100 index is an index of 100 companies selected from 580 companies on the basis of sector leading and market capitalization. It represents almost 80% weight of the total market capitalization of KSE. It reflects different sector company's performance and productivity. It is the performance indicator or benchmark of all listed companies of KSE. So it can be regarded as universe of the study.Non-financial firms listed at KSE-100 Index (74 companies according to the page of KSE visited on 20.5.2015) are treated as universe of the study and the study have selected sample from these companies.

The study comprised of non-financial companies listed at KSE-100 Index and 30 actively traded companies are selected on the bases of market capitalization. And 2015 is taken as base year for KSE-100 index.

3.2 Data and Sources of Data

For this study secondary data has been collected. From the website of KSE the monthly stock prices for the sample firms are obtained from Jan 2010 to Dec 2014. And from the website of SBP the data for the macroeconomic variables are collected for the period of five years. The time series monthly data is collected on stock prices for sample firms and relative macroeconomic variables for the period of 5 years. The data collection period is ranging from January 2010 to Dec 2014. Monthly prices of KSE - 100 Index is taken from yahoo finance.

3.3 Theoretical framework

Variables of the study contains dependent and independent variable. The study used pre-specified method for the selection of variables. The study used the Stock returns are as dependent variable. From the share price of the firm the Stock returns are calculated. Rate of a stock salable at stock market is known as stock price.

RESEARCH METHODOLOGY

The methodology section outline the plan and method that how the study is conducted. This includes Universe of the study, sample of the study, Data and Sources of Data, study's variables and analytical framework. The details are as follows;

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Systematic risk is the only independent variable for the CAPM and inflation, interest rate, oil prices and exchange rate are the independent variables for APT model.

Consumer Price Index (CPI) is used as a proxy in this study for inflation rate. CPI is a wide basic measure to compute usual variation in prices of goods and services throughout a particular time period. It is assumed that rise in inflation is inversely associated to security prices because Inflation is at last turned into nominal interest rate and change in nominal interest rates caused change in discount rate so discount rate increase due to increase in inflation rate and increase in discount rate leads to decrease the cash flow's present value (Jecheche, 2010). The purchasing power of money decreased due to inflation, and due to which the investors demand high rate of return, and the prices decreased with increase in required rate of return (Iqbal et al, 2010).

Exchange rate is a rate at which one currency exchanged with another currency. Nominal effective exchange rate (Pak Rupee/U.S.D) is taken in this study. This is assumed that decrease in the home currency is inversely associated to share prices (Jecheche, 2010). Pan et al. (2007) studied exchange rate and its dynamic relationship with share prices in seven East Asian Countries and concluded that relationship of exchange rate and share prices varies across economies of different countries. So there may be both possibility of either exchange rate directly or inversely related with stock prices. Oil prices are positively related with share prices if oil prices increase stock prices also increase (Iqbal et al, 2012). Atallah (2001) suggested that oil prices cause positive change in the movement of stock prices. The oil price has no significant effect on stock prices (Dash & Rishika, 2011). Six month T-bills rate is used as proxy of interest rate. As investors are very sensitive about profit and where the signals turn into red they definitely sell the shares. And this sensitivity of the investors towards profit effects the relationship of the stock prices and interest rate, so the more volatility will be there in the market if the behaviors of the investors are more sensitive. Plethora (2002) has tested interest rate sensitivity to stock market returns, and concluded an inverse relationship between interest rate and stock returns. Nguyen (2010) studies Thailand market and found that Interest rate has an inverse relationship with stock prices.

KSE-100 index is used as proxy of market risk. KSE-100 index contains top 100 firms which are selected on the bases of their market capitalization. Beta is the measure of systematic risk and has a linear relationship with return (Horn, 1993). High risk

is associated with high return (Basu, 1977, Reiganum, 1981 and Gibbons, 1982). Fama and MacBeth (1973) suggested the existence of a significant linear positive relation between realized return and systematic risk as measured by β . But on the other side some empirical results showed that high risk is not associated with high return (Michailidis et al. 2006, Hanif, 2009). Mollah and Jamil (2003) suggested that risk-return relationship is nonlinear perhaps due to high volatility.

3.4 Statistical tools and econometric models

This section elaborates the proper statistical/econometric/financial models which are being used to forward the study from data towards inferences. The detail of methodology is given as follows.

3.4.1 Descriptive Statistics

Descriptive Statics has been used to find the maximum, minimum, standard deviation, mean and normally distribution of the data of all the variables of the study. Normal distribution of data shows the sensitivity of the variables towards the periodic changes and speculation. When the data is not normally distributed it means that the data is sensitive towards periodic changes and speculations which create the chances of arbitrage and the investors have the chance to earn above the normal profit. But the assumption of the APT is that there should not be arbitrage in the market and the investors can earn only normal profit. Jarque bera test is used to test the normality of data.

3.4.2 Fama-McBeth two pass regression

After the test statistics the methodology is following the next step in order to test the asset pricing models. When testing asset pricing models related to risk premium on asset to their betas, the primary question of interest is whether the beta risk of particular factor is priced. Fama and McBeth (1973) develop a two pass methodology in which the beta of each asset with respect to a factor is estimated in a first pass time series regression and estimated betas are then used in second pass cross sectional regression to estimate the risk premium of the factor. According to Blum (1968) testing two-parameter models immediately presents an unavoidable errors-in-the variables problem. It is important to note that portfolios (rather than individual assets) are used for the reason of making the analysis statistically feasible. Fama McBeth regression is used to attenuate the problem of errors-in-variables (EIV) for two parameter models (Campbell, Lo and MacKinlay, 1997). If the errors are in the β (beta) of individual security are not perfectly positively correlated, the β of portfolios can be much more precise estimates of the true β (Blum, 1968).

The study follow Fama and McBeth two pass regression to test these asset pricing models. The Durbin Watson is used to check serial correlation and measures the linear association between adjacent residuals from a regression model. If there is no serial correlation, the DW statistic will be around 2. The DW statistic will fall if there is positive serial correlation (in worst case, it will be near zero). If there is a negative correlation, the statistic will lie somewhere between 2 and 4. Usually the limit for non-serial correlation is considered to be DW is from 1.8 to 2.2. A very strong positive serial correlation is considered at DW lower than 1.5 (Richardson and smith, 1993).

According to Richardson and smith (1993) to make the model more effective and efficient the selection criteria for the shares in the period are: Shares with no missing values in the period, Shares with adjusted $R^2 < 0$ or F significant (p-value) > 0.05 of the first pass regression of the excess returns on the market risk premium are excluded. And Shares are grouped by alphabetic order into group of 30 individual securities (Roll and Ross, 1980).

3.4.2.1 Model for CAPM

In first pass the linear regression is used to estimate beta which is the systematic risk.

$$R_i - R_f = (R_m - R_f)\beta \quad (3.1)$$

Where R_i is Monthly return of these security, R_f is Monthly risk free rate, R_m is Monthly return of market and β is systematic risk (market risk).

The excess returns $R_i - R_f$ of each security is estimated from a time series share prices of KSE-100 index listed shares for each period under consideration. And for the same period the market Premium $R_m - R_f$ also estimated. After that regress the excess returns $R_i - R_f$ on the market premium $R_m - R_f$ to find the beta coefficient (systematic risk).

Then a cross sectional regression or second pass regression is used on average excess returns of the shares and estimated betas.

$$\hat{R}_i = \gamma_0 + \gamma_1\beta_i + \epsilon \quad (3.2)$$

Where $\lambda_0 =$ intercept, \hat{R}_i is average excess returns of security i , β_i is estimated be coefficient of security i and ϵ is error term.

3.4.2.2 Model for APT

In first pass the betas coefficients are computed by using regression.

$$R_i - R_f = \beta_{i1}f_1 + \beta_{i2}f_2 + \beta_{i3}f_3 + \beta_{i4}f_4 + \epsilon \quad (3.3)$$

Where R_i is the monthly return of stock i , R_f is risk free rate, β_i is the sensitivity of stock i with factors and ϵ is the error term.

Then a cross sectional regression or second pass regression is used on average excess returns of the shares on the factor scores.

$$\hat{R} = \gamma_0 + \gamma_1\beta_1 + \gamma_2\beta_2 + \gamma_3\beta_3 + \gamma_4\beta_4 + \epsilon_i \quad (3.4)$$

Where \hat{R} is average monthly excess return of stock i , $\lambda =$ risk premium, β_1 to β_4 are the factors scores and ϵ_i is the error term.

3.4.3 Comparison of the Models

The next step of the study is to compare these competing models to evaluate that which one of these models is more supported by data. This study follows the methods used by Chen (1983), the Davidson and Mackinnon equation (1981) and the posterior odds ratio (Zellner, 1979) for comparison of these Models.

3.4.3.1 Davidson and MacKinnon Equation

CAPM is considered the particular or strictly case of APT. These two models are non-nested because by imposing a set of linear restrictions on the parameters the APT cannot be reduced to CAPM. In other words the models do not have any common variable. Davidson and MacKinnon (1981) suggested the method to compare non-nested models. The study used the Davidson and MacKinnon equation (1981) to compare CAPM and APT. This equation is as follows;

$$R_i = \alpha R_{APT} + (1 - \alpha)R_{CAPM} + e_i \quad (3.5)$$

Where R_i = the average monthly excess returns of the stock i , R_{APT} = expected excess returns estimated by APT, R_{CAPM} = expected excess returns estimated by CAPM and α measure the effectiveness of the models. The APT is the accurate model to forecast the returns of the stocks as compare to CAPM if α is close to 1.

3.4.3.2 Posterior Odds Ratio

A standard assumption in theoretical and empirical research in finance is that relevant variables (e.g stock returns) have multivariate normal distributions (Richardson and smith, 1993). Given the assumption that the residuals of the cross-sectional regression of the CAPM and the APT satisfy the IID (Independently and identically distribution) multivariate normal assumption (Campbell, Lo and MacKinlay, 1997), it is possible to calculate the posterior odds ratio between the two models. In general the posterior odds ratio is a more formal technique as compare to DM equation and has sounder theoretical grounds (Aggelidis and Maditinos, 2006).

The second comparison is done using posterior odd ratio. The formula for posterior odds is given by Zellner (1979) in favor of model 0 over model 1.

The formula has the following form;

$$R = [ESS_0/ESS_1]^{N/2} N^{K_0-K_1/2} \quad (3.6)$$

Where ESS_0 is error sum of squares of APT, ESS_1 is error sum of squares of CAPM, N is number of observations, K_0 is number of independent variables of the APT and K_1 is number of independent variables of the CAPM. As according to the ratio when; $R > 1$ means CAPM is more strongly supported by data under consideration than APT. $R < 1$ means APT is more strongly supported by data under consideration than CAPM.

IV. RESULTS AND DISCUSSION

4.1 Results of Descriptive Statics of Study Variables

Table 4.1: Descriptive Statics

Variable	Minimum	Maximum	Mean	Std. Deviation	Jarque-Bera test	Sig
KSE-100 Index	-0.11	0.14	0.020	0.047	5.558	0.062
Inflation	-0.01	0.02	0.007	0.008	1.345	0.510
Exchange rate	-0.07	0.04	0.003	0.013	1.517	0.467
Oil Prices	-0.24	0.11	0.041	0.060	2.474	0.290
Interest rate	-0.13	0.05	0.047	0.029	1.745	0.418

Table 4.1 displayed mean, standard deviation, maximum minimum and jarque-bera test and its p value of the macroeconomic variables of the study. The descriptive statistics indicated that the mean values of variables (index, INF, EX, OilP and INT) were 0.020, 0.007, 0.003, 0.041 and 0.047 respectively. The maximum values of the variables between the study periods were 0.14, 0.02, 0.04, 0.41, 0.11 and 0.05 for the KSE- 100 Index, inflation, exchange rate, oil prices and interest rate.

The standard deviations for each variable indicated that data were widely spread around their respective means.

Column 6 in table 4.1 shows jarque bera test which is used to check the normality of data. The hypotheses of the normal distribution are given;

H_0 : The data is normally distributed.

H_1 : The data is not normally distributed.

Table 4.1 shows that at 5 % level of confidence, the null hypothesis of normality cannot be rejected. KSE-100 index and macroeconomic variables inflation, exchange rate, oil prices and interest rate are normally distributed.

The descriptive statistics from Table 4.1 showed that the values were normally distributed about their mean and variance. This indicated that aggregate stock prices on the KSE and the macroeconomic factors, inflation rate, oil prices, exchange rate, and interest rate are all not too much sensitive to periodic changes and speculation. To interpret, this study found that an individual investor could not earn higher rate of profit from the KSE. Additionally, individual investors and corporations could not earn higher profits and interest rates from the economy and foreign companies could not earn considerably higher returns in terms of exchange rate. The investor could only earn a normal profit from KSE.

Table 1 Table Type Styles


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I. ACKNOWLEDGMENT

The preferred spelling of the word “acknowledgment” in America is without an “e” after the “g”. Avoid the stilted expression, “One of us (R.B.G.) thanks...” Instead, try “R.B.G. thanks”. Put applicable sponsor acknowledgments here; DONOT place them on the first page of your paper or as a footnote.

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