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# Development of Economic UV Spectrophotometric Method for Determination of Linagliptin in its Ternary Mixture with Empagliflozin and Metformin: Comparison to Economic Pharmaceutical Analysis in Literature

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## ABSTRACT

*A new economic UV spectrophotometric method was developed using methanol as a solvent to determine linagliptin in its ternary mixture with empagliflozin and metformin either in bulk or in different FDA approved pharmaceutical formulations, namely Tradjenta® (linagliptin), Jentadueto® (linagliptin and metformin) and Glyxambi® (linagliptin and empagliflozin) tablets. Determination of linagliptin at 296 nm was proved to be linear in the range of 5.0–25.0 µg/mL, and exhibited good recovery (97.88–102.11%). The results were in good agreement with the label claims. The obtained results proved that the method can be employed for the routine analysis of the commercial formulations.*

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## INTRODUCTION

Linagliptin is a dipeptidyl-peptidase-4 inhibitor for the treatment of type 2 diabetes. Three pharmaceutical formulations were approved by FDA namely Tradjenta® (linagliptin), Jentadueto® (linagliptin and metformin) and Glyxambi® (linagliptin and empagliflozin) tablets. Literature survey reveals that many methods were developed for determination of linagliptin [1-18] but no spectrophotometric method was reported in the literature for determination linagliptin in its ternary mixture with empagliflozin and metformin. Thus, the aim of the present work was to develop a new economic UV spectrophotometric method to determine linagliptin in its ternary mixture with empagliflozin and metformin either in bulk or in different FDA approved pharmaceutical formulations. Spectrophotometry, because of its low cost, it has long been applied for the economic analysis of many drugs as an alternative for complex instrumentation methods. The importance of economic analysis has been increased dealing with some aspect of what might be termed an "economic analytical approach". The array of simple economic different analytical procedures in the literature [19-56] points to the negotiable limits of this hugely open category in developing countries in the previous five years (2012-2016).

## MATERIALS AND METHODS

Aliquots from linagliptin methanolic stock solution (1 mg/mL) equivalent to 50-250 µg were transferred into a set of 10 mL volumetric flasks and completed to volume with methanol to prepare calibrators equivalent to 5-25 µg/ml. The zero order absorption of each solution was recorded against methanol as a blank at 296 nm, then plotted against its corresponding concentration and the regression parameters were computed and found to be (Absorbance = 0.0257 Concentration - 0.0089 with r = 0.999). Also, the absorption spectrum was recorded for the laboratory prepared mixture containing 10 µg/ml of each drug, against methanol as a blank (figure 1). The zero order absorption spectra at 296 nm were used for the direct determination of linagliptin. The concentration of linagliptin was calculated from the corresponding regression equation and found to be 99.64 %. Moreover, accuracy was checked by repeating the procedure using three different concentrations and found to be between 97.88 % and 102.11 %. Also fifty milliliters of methanol were added to weighed amount of the finely powdered Tradjenta®, Jentadueto® and Glyxambi® tablets equivalent to 10 mg linagliptin of each extract, sonicated for 15 min and then made up to 100 ml with methanol

separately for each formulation and then filtered and then 1 ml of each diluted extract was further diluted with methanol in 10 ml volumetric flask separately. Zero order absorption spectra at 296 nm were used for the direct determination of linagliptin. The concentrations of linagliptin was calculated from corresponding regression equation and found to be in the range of 99.31 % to 101.05 %.

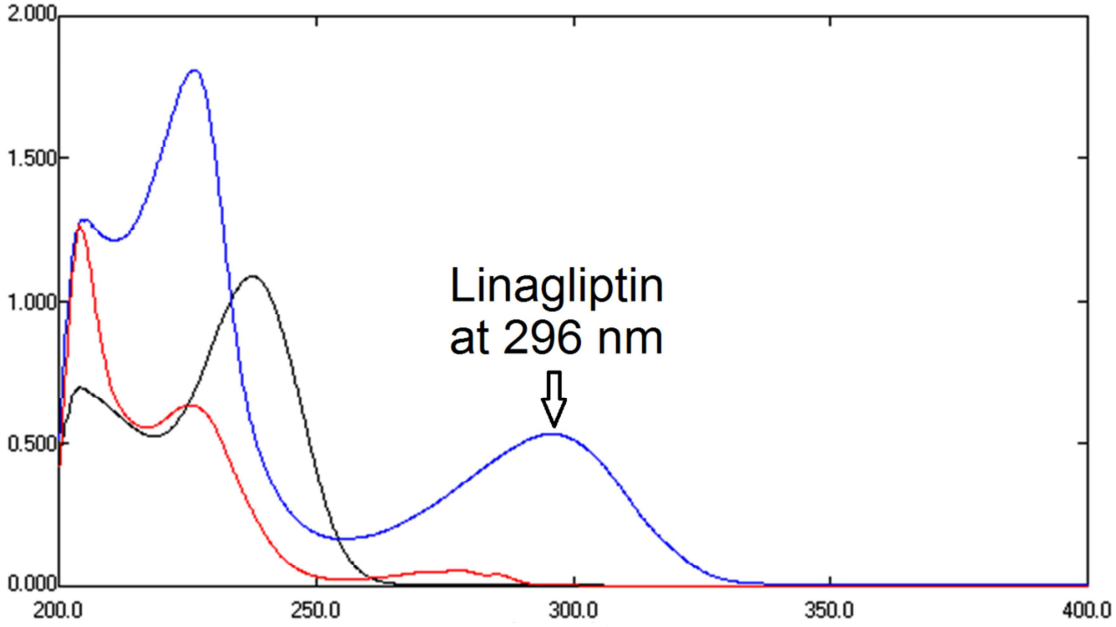


**Figure 1: Zero order spectra of 10 µg/ml linagliptin, 10 µg/ml metformin and 10 µg/ml empagliflozin**

Literature review offered many economic alternatives for drug control with many practical applications as an attempt to highlight the concept and basics of simple pharmaceutical analysis without complex instrumentation using cost-effective drug assays. Many papers were selected [19-56] to be considered as a guide for the researchers interested in low cost analytical techniques in developing countries and highlighted a variety of analytical techniques that have been applied in the analysis of pharmaceuticals as an "economic analytical approach". Economic analysis provides the quality control laboratory professionals with a comprehensive tool for sound management of the quality control function using analytical processes characterizing the quality of statistical control procedures; predicting the quality of an analytical process; predicting the productivity of an analytical process; selecting and designing cost-effective quality control procedures. The main magnifying objectives were to obtain a large amount of chemical information of a high quality, and its main reducing objectives to use less material (sample, reagents), time and human resources with minimal costs and risks for analysts and the environment. The present work and the proposed techniques [19-56] were characterized by expeditiousness of the analytical methods due to its ability to rapidly develop the analytical process from raw sample to results. Expeditiousness is often expressed as the sample frequency (i.e. in samples per hour or per day). Also personnel-related factors were considered including the risks associated to the use of analytical tools and the analyst's safety and comfort.

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