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Sildenafil Pharmacokinetic Interactions with Ciprofloxacin and Clarithromycin

A Thesis Submitted
For the Partial Fulfillment of The Master Degree in Pharmaceutical Sciences (Clinical Pharmacy)

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٢٠٠٧

بسم الله الرحمن الرحيم

{ الْحَمْدُ لِلّهِ الَّذِي هَدَانَا لِهَذَا وَمَا كُنَّا لِنَهْتَدِيَ لَوْلا أَنْ هَدَانَا اللّهُ }

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INTRODUCTION

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INTRODUCTION

Sildenafil (Viagra®, Pfizer) was approved by the Food and Drug Administration (FDA) on March ٢٧, ١٩٩٨, as the first oral therapeutic agent for the management of male erectile dysfunction, a condition that affects ١٠% of all males and becomes more common with age (Boolell et al., ١٩٩٦ and Goldstein et al., ١٩٩٨).

١.General properties of sildenafil:

١.١ Chemical Structure:

Sildenafil is chemically designated as ١-[[٣-(٦,٧-dihydro-١-methyl-٧-oxo-٣-propyl-١H-pyrazolo[٤,٣-d]pyrimidin-٥-yl)-٤-ethoxyphenyl]sulfonyl]-٤-methyl piperazine and has the following structural formula:

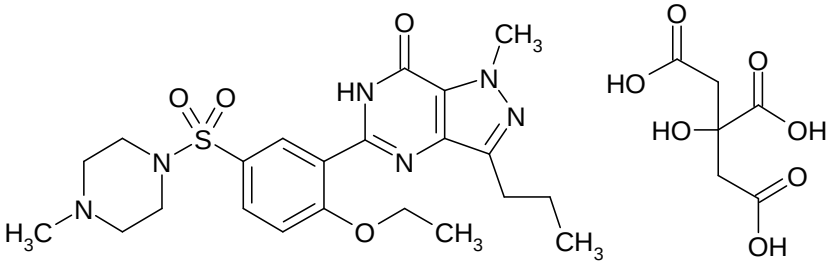

Figure (I-١): The chemical structure of sildenafil citrate.

Sildenafil is a pyrazolopyrimidinone derivative similar in structure to the guanosine base of cyclic guanosine monophosphate (cGMP), the endogenous ligand of the phosphodiestrase enzyme (PDE) type ٥ isoenzyme. The propyl, methyl and ethoxyl groups of pyrazolopyrimidinone nucleus enhances the specificity of sildenafil for PDE type ٥ compared to PDE types ١ and ٣ isoenzymes (Terrett et al., ١٩٩٦).

١.٢. Physicochemical properties:

Sildenafil is commercially available as sildenafil citrate salt, however the dosages and concentrations are expressed in terms of the base. Sildenafil citrate is white to off-white crystalline powder. It has an aqueous solubility of ٣.٥ mg/ml, molecular weight of ٦٦٦.٧ and the drug is moderately lipophillic (Waiker et al., ١٩٩٩). Sildenafil has basic functional groups with a pKa value of ٨.٧ although a weak acidic moiety is also present on the parent compound (Cooper et al., ١٩٩٧).

١.٣. Therapeutic Indications:

Sildenafil is the first oral therapeutic agent introduced for the treatment of erectile dysfunction (ED), a state of inability to achieve or maintain an erection sufficient for satisfactory sexual performance (NIH Consensus, ١٩٩٣). This disease affects an estimated ١٠% of the adult male population and becomes progressively with age (Feldman et al., ١٩٩٤).