Preparation, Characterization, and Antifungal activity of Sertaconazole-Sulfobutyl ether -β-Cyclodextrin Complex

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A Thesis

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جامـــــــعة الاســـــــــراء

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Dedication

This thesis is dedicated to my parents, my husband and my lovely family. My parents, the source of my happiness and success in my life, who have always been supportive anytime I needed their support, without them I would have been unable to accomplish this competitive phase of education. To my husband, because of your love, acceptance, patience and encouragement that has been seen through our first year of marriage and my last year of thesis. I will appreciate all you have done for me. To my sisters and my brothers for funny times I spent it with them after feeling tired and frustrated. To my little girl Eleen, my Soul, you are the joy of my life and I love you forever.

I also dedicate this thesis to my friends for happy and hard times we went through together during our Master's journey.

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LIST OF ABBREVIATIONS OR SYMBOLS

Abbreviation or symbols	Definition
SER	Sertaconazole
HP-β-CD	Hydroxy propyl-β-cyclodextrin
SBE-β-CD	Sulfobutyl ether- β-cyclodextrin
CD	Cyclodextrin
DSC	Differential scanning calorimetry
FT-IR	Fourier Transform infrared spectroscopy
XRD	X-ray diffraction
PH	Potency of hydrogen
Cps	Centi poises
DT	Disintegration time
Kg	Kilogram
PEG	Polyethylene glycol
C. albicans	*Candida albicans*
G	Gram
Ml	Milliliter
ATCC	American type culture collection
Na CMC	Sodium carboxymethyl cellulose
HPMC	Hydroxhypropyl methyl cellulose
NaOH	Sodium hydroxide
SD	Standard deviation
Min	Minute
T	Time
CFU	Colony Forming Unit

Hr	Hour
UV-Vis	UV-Visible spectroscopy
DV	Displacement value
RPM	Revolution per minute
Mix	Mixture
M wt	Molecular weight
H.V.S	High vaginal swab
MR	Melting range
β-CD	Beta cyclodextrin

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ABSTRACT

Background: Vaginal candidiasis is one of the most common infections in women. A large variety of antifungal drugs are used for treatment. Sertaconazole (SER) is an imidazole derivative used for treatment of local and systemic fungal infections. Sertaconazole has poor water solubility which affects its dissolution and bioavailability. The objective of this study was to enhance the dissolution and therapeutic efficacy of SER through interaction with certain cyclodextrins (CD) namely HP-β-CD and SBE-β-CD. This could also improve the overall drug efficiency toward *C. albicans*. In addition, the optimum system in terms of higher *in vitro* release was formulated into vaginal suppositories and topical hydrogels for maximum effect.

Methods: Inclusion complex of SER and CD either HP-β-CD or SBE-B-CD were prepared by physical mixture, ground mixture and co-evaporated at 1:1 and 1:2 molar ratios. Systems were characterized by Fourier Transform infrared spectroscopy (FT-IR), differential scanning calorimetry (DSC), X-ray diffraction (XRD) and *in vitro* dissolution studies. SER hydrogels were formulated in different gelling agents and evaluated for their pH, viscosity, homogeneity, *in vitro* drug release, drug content and antifungal activities. SER vaginal suppositories were formulated using hydrophilic and hydrophobic bases and evaluated for their hardness, disintegration time, drug content, melting point and *in vitro* drug release.

Results: Results obtained from FT-IR, DSC, XRD and *in vitro* dissolution studies showed that the co-evaporation method was the best method for forming the inclusion complex with the investigated CDs. SER was released from SER/ SBE-β-CD co-evaporate complex at 1:2 molar ratio at a percentage of 93.87%±0.049. Hydrogel 1% and vaginal suppositories of 100 mg SER were successfully formulated and showed SER release of 95.42%±0.148 and 96.31%±0.37 respectively.

Conclusion: SER inclusion complex with SBE-β-CD enhanced the dissolution of the drug significantly. In addition, the optimum hydrogel formulation showed significant antifungal activity against *C. albicans* compared with hydrogel containing SER alone.