Faculty of Science

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Synthesis of some benzothiazole and benzothiazine derivatives with expected biological activity

Thesis

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Approval Sheet

Synthesis of some benzothiazole and benzothiazine derivatives with expected biological activity

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CONTENTS

List of abbreviations

DABCO	:1,4-diazobicyclo(2,2,2)octane
DMAP	**:** 4-Dimethylaminopyridine
PSDIB	: Poly (4-diacetoxyiodo)styrene
HepG2	**:** Human hepato cellular liver carcinoma
MCF-7	**:** Human breast adeno carcinoma cell line
PC3	**:** Human prostate cancer cell line
A431	**:** Human squamous carcinoma cell line
A373	**:** Human malignant melanoma 1L-1 Sensitive
Bcap37	**:** Human breast cancer cell line
CoMFA	**:** Comparative molecular field analysis
CoMSIA	**:** Comparative molecular similarity indices analysis
IC_{50}	: Inhibition concentration

ENGLISH SMMARY

SUMMARY

This work illustrates the versatile role of benzothiazolone and benzothiazinone moieties in the synthesis of different heterocyclic systems from readily obtainable materials and evaluation of their antifungal and antibacterial activities.

The work can be divided into three main parts:-

i- First part: deals with reactions of benzothiazolone derivative

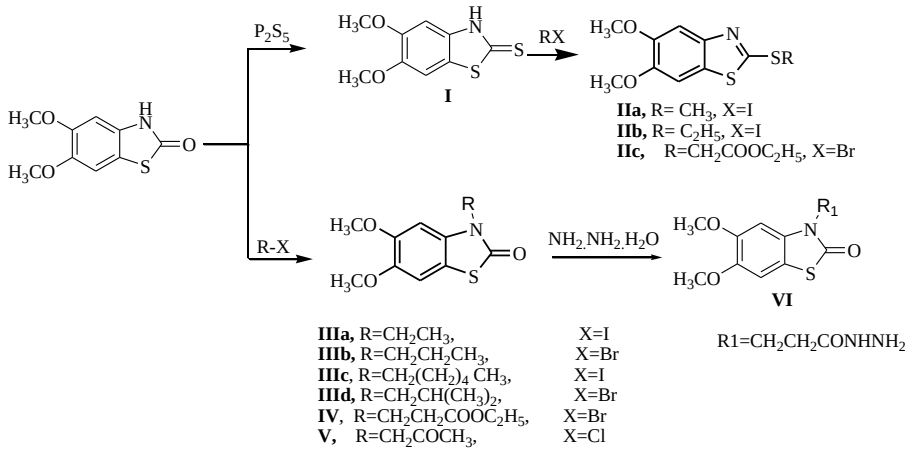
ii- Second part: deals with reactions of benzothiazinone derivative

iii- Third part: antimicrobial evaluation

i- <u>First part</u>: Different reactions of benzothiazolone derivative.

Thiation of 5,6-dimethoxy-3*H*-benzothiazol-2-one afforded 5,6-dimethoxybenz[*d*]thiazole-2(3*H*)-thione **(I)**, which was alkylated with different alkyl halides such as: methyl or ethyl iodide and / or bromo ethylacetate to give the corresponding S-alkyl derivatives **IIa-c**. Direct reaction of the benzothiazolone derivative with different alkyl halides such as: ethyl iodide /bromo propan/ iodo hexane/ iso butyl bromide/ ethyl 3- bromopropanoate and chloroacetone led to the formation of the corresponding N-alkyl derivatives **IIIa-d, IV, V**, respectively. The target compound, propanhydrazide derivative **VI** was constructed

by hydrazinolysis of the propanoate compound **IV** by hydrazine hydrate in boiling ethanol [cf. scheme 1].



Scheme 1

Reaction of propanhydrazide derivative **VI** with dichloromaleic anhydride and / or isatin gave the propanamide and benzothiazolone derivatives **VII, VIII** respectively.

The new benzothiazolone derivatives containing different substituted pyrazole rings **IX** and **X** have been formed *via* the reaction of propanhydrazide derivative **VI** with acetyl acetone and / or 2-ethoxymethylene-cyanoacetate, respectively.

When the propan hydrazide **VI** was allowed to react with triethylorthoformate, ammonium thiocyanate, methyl isothiocyanate and carbon disulfide gave N-ethoxy

methylenepropane-hydrazide **XII**, mercaptotrizole **XIII,** methylthio-semicarbazide **XIV** and / or the oxadiazoline thione **XV** derivatives respectively.

The structure of oxadiazoline thione derivative **XV** was chemically proved *via* its reaction with hydrazine hydrate and / or 4-(2-chloroethyl)morpholine hydrochloride to give amino triazolthione **XVI** and morpholinoethylthiooxadiazol **XVII** compounds respectively [cf. Scheme 2].