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## Nano-structured complexes of reserpine and quinidine drugs with chloranilic acid based on intermolecular H-bond: Spectral and surface morphology studies



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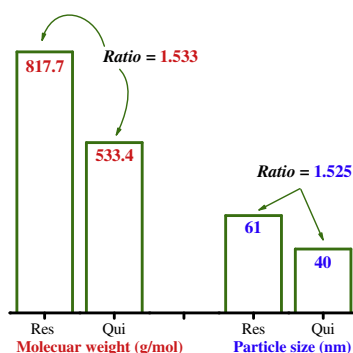
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### HIGHLIGHTS

- Complexes of reserpine and quinidine with chloranilic acid were obtained.
- IR measurements confirmed the existing of intermolecular H-bond.
- Microstructure properties of the reported complexes were observed.
- Debye–Scherrer equation indicates that complexes are in the nano-range.
- One of the complex exhibited a remarkable morphology feature.

### GRAPHICAL ABSTRACT

The interesting correlation between molecular weight and particle size of the reported complexes.



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### ABSTRACT

The study of the drug-acceptor interaction may be useful in understanding the drug-receptor interactions and the mechanism of drug action. Here, complexes of reserpine (Res) and quinidine (Qui) drugs with chloranilic acid (CLA) have been synthesized. Then, these complexes were characterized chemically and structurally using CHN elemental analysis, infrared (IR) and electronic absorption spectroscopy, X-ray diffraction (XRD) and scanning electron microscopy (SEM). The stoichiometry of the H-bonded complex was found to have a 1:1 ratio, so these complexes can be formulated as [(Drug)(CLA)]. IR measurements confirmed the presence of intermolecular H-bond. Application of Debye–Scherrer equation indicates that the formed complexes are in the range of nano-size. The Res complex exhibits a remarkable crystalline morphology. It was also found that the particle size of Res complex is 1.533 time higher than that of Qui complex. Interestingly, free Res molecular weight is higher than that of free Qui by the same ratio (precisely; 1.525).

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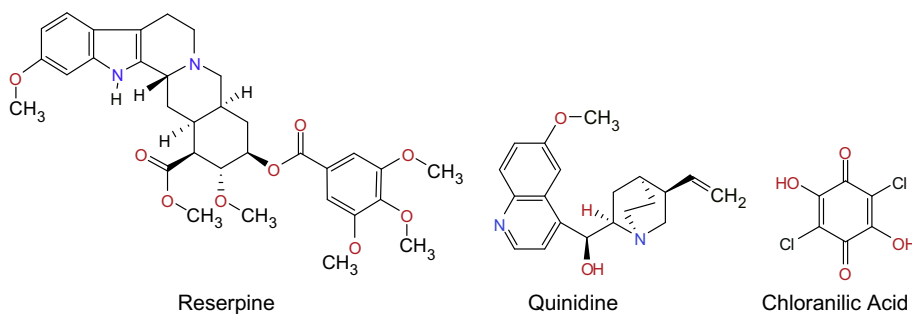
### Introduction

Recently, there has been a great deal of interest in the formation of stable charge-transfer, proton-transfer or H-bonded complexes

that result from the reaction between acceptors and drugs or biological compounds. This is because of the significant physical and chemical properties of these complexes. The drug-acceptor complexation is an important technique that is cheaper, simpler, and more efficient than the methods of drug determination described in the literature. The study of the drug-acceptor

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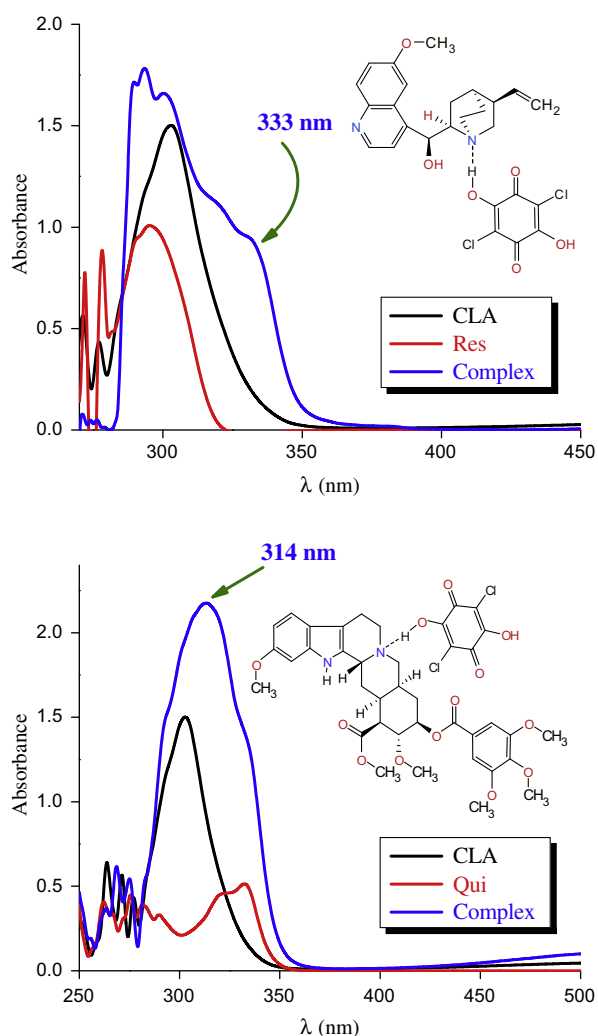
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**Scheme 1.** The chemical structures of Res, Qui and CLA.

**Table 1**  
Spectroscopic data for the H-bonded complexes in methanol at room temperature.

Complex	Color	Absorption (nm)	Stoichiometry (Drug-CLA)	$K$ (L mol <sup>-1</sup> )	$\epsilon_{\max}$ (L mol <sup>-1</sup> cm <sup>-1</sup> )
[(Res)(CLA)]	Reddish brown	333	1:1	$1.69 \times 10^4$	$1.23 \times 10^4$
[(Qui)(CLA)]	Dark brown	314	1:1	$1.16 \times 10^7$	$2.38 \times 10^4$



**Fig. 1.** Electronic absorption spectra of [(Res)(CLA)] and [(Qui)(CLA)] complexes in methanol solvent.

complexation may be useful in understanding the drug-receptor interactions and the mechanism of drug action. Furthermore, the crystalline drug-acceptor complexes have a vital role in biological systems such as antimicrobial activity and DNA-binding. Furthermore, literature shows that these complexes exhibit potential antimicrobial properties against Gram-positive and Gram-negative bacteria as well as fungi [1–11]. Herein, the drug-acceptor interaction between the drug reserpine and quinidine with chloranilic acid (CLA) acceptor was reported. Reserpine (Res), chemically methyl (3 $\beta$ , 6 $\beta$ , 17 $\alpha$ , 18 $\beta$ , 20 $\alpha$ )-11,17-dimethoxy-18-[(3,4,5-trimethoxybenzoyl) oxy]yohimban-16-carbox-ylate, the structure of which is shown in [Scheme 1](#), is an indole alkaloid antipsychotic and antihypertensive that exists at room temperature as a white or pale-buff to yellow odorless powder [12]. Res is a biologically active naturally occurring drug and is now largely used to lower blood pressure, reduce the heart rate, relief of psychotic symptoms and as a tranquilizer and sedative in humans [13,14]. Quinidine (Qui), chemically (9S)-6'-methoxycinchonan-9-ol, the structure of which is shown in [Scheme 1](#), is a pharmaceutical agent that acts as a class I antiarrhythmic drug in the heart [15]. It is a stereoisomer of quinine, originally derived from the bark of the cinchona tree. Qui is well-known as medicinally important compound [16]. Based on the interesting results obtained for the complexation properties of drug-acceptor, in this research herein, as a continuation of my works in this field [17–19], the H-bonded complexes of Res and Qui with CLA were synthesized and spectroscopically investigated in both solution and solid state. The complexes have been structurally characterized via CHN elemental analysis; infrared (IR) and electronic absorption spectroscopy; powder X-ray diffraction; and scanning electron microscopy (SEM).

## Materials and methods

### Reagents and solutions

All reagents and chemicals used throughout this study were of analytical reagent grade and all solutions were freshly prepared daily. Methyl (3 $\beta$ , 6 $\beta$ , 17 $\alpha$ , 18 $\beta$ , 20 $\alpha$ )-11,17-dimethoxy-18-[(3,4,5-trimethoxybenzoyl) oxy]yohimban-16-carbox-ylate (Res; C<sub>33</sub>H<sub>40</sub>N<sub>2</sub>O<sub>9</sub>; 608.68) and (9S)-6'-methoxycinchonan-9-ol, (Qui; C<sub>20</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub>; 324.417) were purchased from Merck Chemical

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