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SYNTHESIS OF CHITOSAN SCHIFF BASES OF ZIPRASIDONE, ONDANSARTAN AND P-HYDROXY BENZALDEHYDE FOR PHARMACETICAL APPLICATIONS

K. Lakshmi *, M. Kishore Babu, M. Sucharitha, B.Vara Lakshmi, T.Vijaya Lakshmi

Sri Siddhartha Pharmacy College, Nuzvid, Krishna district-521201

*Corresponding author E-mail: lakshmikakunuri95@gmail.com

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ABSTRACT

Objective: The objective of the present study is to synthesis schiff's bases of chitosan by reacting with carbonyl containing group of ziprasidone, ondansartan and p-hydroxy benzaldehyde at elevated temperature in slightly acidic conditions and to characterize the compounds by using FT-IR spectroscopy. **Methods:** We have to synthesis schiff's base of different carbonyl containing group of drugs by using reflux method and have to identifided the peaks of newly formed compounds by using FT-IR spectroscopy. **Results:** Chitosan with ziprasidone gives peaks at 1748 cm^{-1}**.** The chitosan with ondansartan give peak at 1623cm^{-1} and there is no peak was found the chitosan with p-hydroxy benzaldehyde. **Conclusion:** The formed schiff's base product increases the bioavailability of the drug and decreases the adverse effects of drug because chitosan is the neutral compound and should not show any side effects because it is a naturally occurring compound. Chitosan is the non- toxic, harmless compound and it can be used for the further formulation. We conclude that the formation of schiff's base with ziprasidone, ondansartan, p-hydroxy benzaldehyde is strongly stable products.

INTRODUCTION

Chitosan is a natural linear bio-polyaminosaccharide is derived by the alkaline deacetylation of chitin, which is the major component of protective cuticles of various crustaceans like crabs, shrimps, prawns, lobsters and cell walls of some fungi such as aspergillus and mucor. Chitosan is cheap, biodegradable and nontoxic to mammals. This makes it applicable for use as an additive in food industry, as a hydrating agent in cosmetics, more recently as pharmaceutical agent in preparation of biomedicine and as antimicrobial agent in clinical application. Chitosan is weak base and insoluble in water and organic solvent. However it is soluble in dilute aqueous acidic medium (pH < 6.5). It gets precipitated in alkaline solution or with the poly anions and forms gel at low p^H (Ambore S. M et al., 2013). It is a modified non-toxic carbohydrate polymer derived from chitin through enzymatic or chemical deacetylation. It is formed by β-(1, 4) glucosamine units as its main component (> 80%) and N-acetyl glucosamine (< 20%) distributed randomly along the chain, forming a very complex chemical web (Guerra-Sanchez et al., 2017).

Properties of Chitosan: It has a molecular weight average between 50 and 150 KDa, with a p^{Ka} value of 6.3 and is soluble in dilute acid solutions. At this p^H, chitosan behaves as a

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large polycationic molecule due to its reactive amino groups, which make its use in industry and research in a variety of fields possible (Guerra-Sanchez et al., 2017).

Applications of Chitosan :-[3]

Pharmaceutics:-

- Gels, hydrogels (controlled and sustained drug release).
- Films and membranes (controlled drug release).
- Emulsions (microspheres, microcapsules), (sustained drug release, increased bioavailabity, mucoadhesion).
- Targeted cancer therapy (retention and accumulation of drug in tumour).
- Systems for controlled delivery /release of peptide drugs, vaccines, genes.

Medicine and biomedicine:-

- Wound dressings, wound treatment, bandages.
- Sutures, surgical implants.
- Haemodialysis membranes, biomedical devices coatings.
- Haemostatics, anticoagulants.

Tissue engineering: Scaffolds for tissue engineering, artificial skin grafts.

Others: Agriculture, food industry, textile industry, waste water treatment.

MATERIALS AND METHODS:

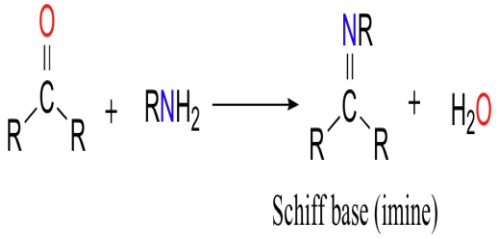
Chemicals: Chitosan, acetic acid, ethanol, ethyl acetate and chloroform.

Drugs: Ziprasidone, ondansartan and p-hydroxy benzaldehyde.

Apparatus: Round bottom flask, 100 ml volumetric flask, beakers, pipette, reflux condenser, heating pan.

Equipment: FT-IR spectroscopy

REACTION OF SCHIFF'S BASE: Schiff bases are the condensation products (following reaction -1) of primary amines and carbonyl compounds, named after **Hugo Schiff**, who discovered them in **1864** (Bharati et al., 2017). The electrophonic carbon atoms of aldehyde and ketones can be targets of nucleophilic attack by amines. The end result of this reaction is a compound in which the C=O. double bond is replaced by a C=N double bond. This type of compound is known as an imine (or) schiff base [5].

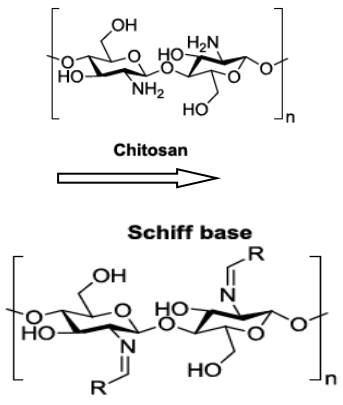


Reaction -1:- General reaction of formation of schiff base [5].

SCHIFF'S BASE SYNTHESIS BY USING REFLUX METHOD :-[6]

The imine formation was set to 24 hours in ethanol at 0.12 Molar acetic acid and the reduction step was set to 24 hours was carried out at different pH and solvents to establish the optimal reaction conditions.

Acetic acid (CH_3COOH) Ethanol (C_2H_5OH), P^H-3.1, 24 hours. at room temperature.



Reaction -2:- Schiff's base synthesis.

Preparation of 0.12 Molar acetic acid solutions: 0.75ml of acetic acid was dissolved in 100 ml of water to produce 0.12 Molar acetic acid solutions.

Scheme 1:- Preparation of ziprasidone with chitosan:-

Procedure: 1 Mole of chitosan (500mg) was dissolved in 45 ml of 0.12 Mole acetic acid, add 2 Moles (1.22 mg) of drug (ziprasidone) and add 33ml of ethanol to increase solubility. Maintained the p^H 3.1. After 24 hours reflux the mixture about 1 hour and dried. The formed product is pinkish color crystalline substance.

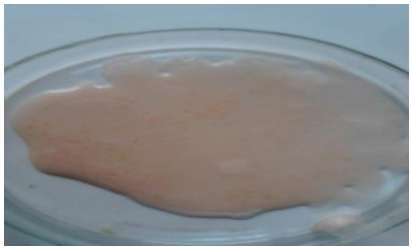


Figure1:- Pinkish color crystalline substance.

Scheme 2: Preparation of ondansartan with chitosan:

Procedure: 1 Mole of chitosan (500 mg) was dissolved in 35 ml of 0.12 Mole acetic acid, add 2 Moles (0.87gm) of drug (ondansartan) and add 22 ml ethanol to increase solubility. Maintained the P^H 3.1. After 24 hours reflux the mixture about 1hour and dried. The formed product is white color flakes.

Figure2: White color flakes.

Scheme3: Preparation of p-hydroxy benzaldehyde with chitosan:

Procedure: 1 Mole of chitosan (500mg) was dissolved in 35 ml of 0.12 Mole of acetic acid, add 2 Moles (0.36gm) of drug (P-Hydroxy benzaldehyde) and add 23 ml of ethanol to increase solubility. Maintained the P^H 3.1 after 24 hours reflux the about 1 hour and dried. The formed product is colorless flakes.

Figure3: Colorless flakes.

Fourier Transform Infrared (FTIR) Spectroscopy Testing: FTIR spectroscopy was used to understand the functional groups and its molecular bond structure in the range of 4000 cm-1 to 400 cm-1. The FTIR spectroscopy with a model name of 'IRAffinity-1' was used and equipped by Shimadzu (Japan) Corporation. Approximately 0.5 mg of powder sample was mixed with approximately 100 mg of dry powder, potassium bromide (KBr) in a small agate pestle to create a sample pellet for FTIR spectroscopy. Then, the mixture sample pellet was then taken into the sample holder inside the spectroscopy. Vacuum pressure was applied onto the mixture sample pellet inside the spectroscopy. The vacuum pressure causes the removal of moisture inside spectroscopy. IR spectrum bands were obtained when laser of infrared projected onto the mixture pellets. All the information obtained was analyzed according to ASTM E168-06 and ASTM E168-06 standards (et al .,)

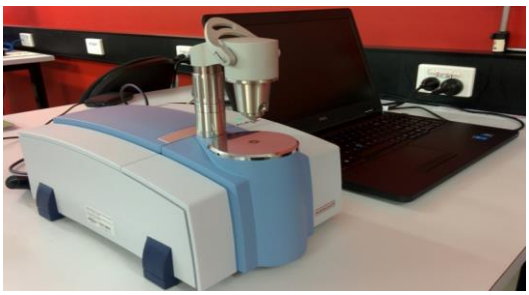
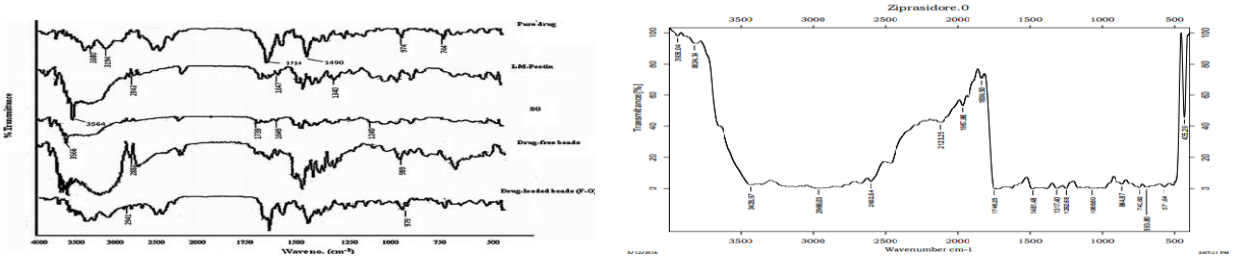


Figure 4: FT-IR Spectroscopy

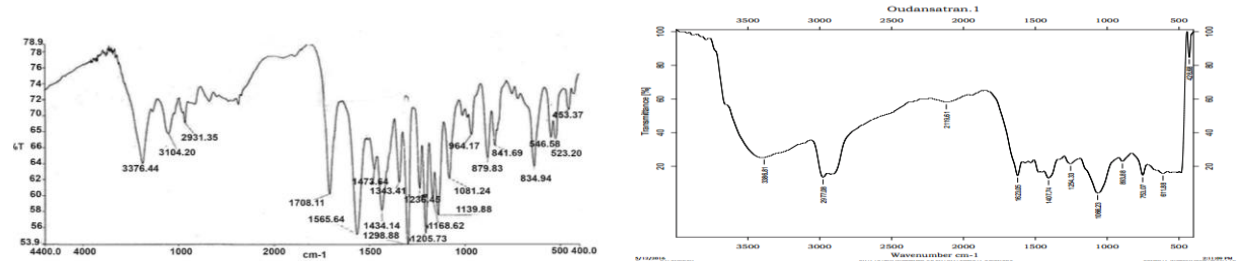
Table: 1- FT-IR technique, the following data was obtained

S.no	Drug name	Pure peak(cm^{-1})	Product peak(cm^{-1})
1	Ziprasidone	1714	1748
2	Ondansartan	1637	1623
3	P-Hydroxy Benzaldehyde	1649	No peak

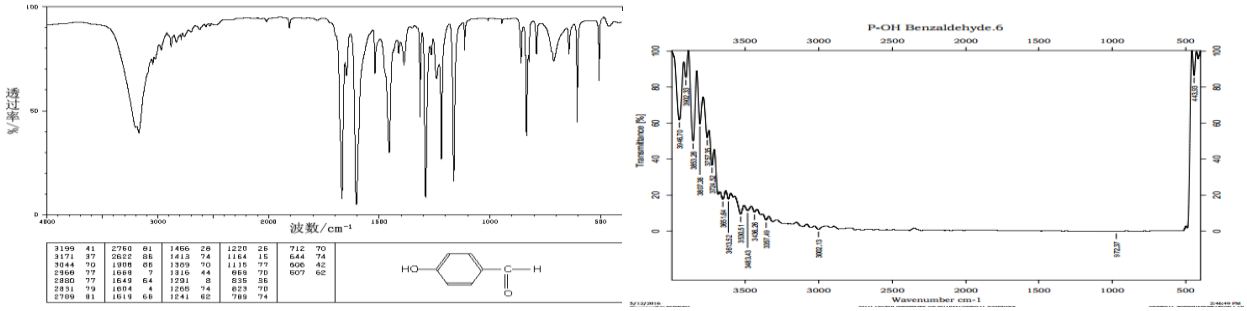
1. Ziprasidone: Pure drug C=O peak at 1714 cm-1, Product peak at 1748 cm-1



2. Ondansartan: pure drug C=O peak at 1637 cm-1, product peak at 1623 cm-1



3. P-Hydroxy Benzaldehyde: pure C=O peak at 1649 cm-1, product No peak found



CONCLUSION:

The synthesis of schiff's base with ziprasidone, ondansartan, p-hydroxy benzaldehyde. FT-IR techniques as stated above and the chitosan with ziprasidone give peaks at 1748 cm^{-1}**.** The chitosan with ondansartan give peak at 1623cm^{-1} and there is no peak was found the chitosan with p-hydroxy benzaldehyde. From above data schiff base with ziprasidone, ondansartan, p-hydroxy benzaldehyde was formed and it will be use for the pharmaceutical applications. The formed schiff base product increases the bioavailability of the drug and decreases the adverse effects of drug because chitosan is the neutral compound and should not show any side effects because it is a naturally occurring compound. Chitosan is the non-toxic. Harmless compound and it can be used

for the further formulation. Finally we conclude that the formation of schiff base with ziprasidone, ondansartan, p-hydroxy benzaldehyde is strongly stable products.

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