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AN OVERVIEW OF SOLUBILITY OF CLASS - II DRUGS BY FTIR ANALYSIS

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Abstract: The aim of the present work is to study the solubility of class-II drugs by FTIR analysis. Avanafil is a PDE5 inhibitor approved for erectile dysfunction by the FDA. Avanafil is sold under the brandnames Stendra and Spedra. Avanafil is a class-II drug. Class-II drug are Low Solubility and High Permeability Solubility of Pure drug is studied with various Excipients. Alteration of solubility is observed by using FTIR analysis and solubility studies. Higher amino acids are insoluble in water. Avanafil contains more number of amine groups which in turn increases the molar mass of the compound therefore it is low soluble in water. The obtained results indicate that the solubility of class-II drug i.e AVANAFIL was enhanced when it is mixed with the Excipient Co-Povidine. The Co-Povidine reacts with Avanafil alters the higher amines in Avanafil which increases the polarity of the drug. Co-Povidine also converts the alkenes present in Avanafil which enhances the solubility.

IndexTerms **- Avanafil, Solubility, Co-Povidine, Class -II Drugs.**

I. INTRODUCTION

FOURIER TRANSFORM INFRARED SPECTROPHOTOMETER (FTIR)[(1,2)]

A spectrometer is an optical instrument used to measure properties of light over a specificportion of the electromagnetic spectrum, 5 microns to 20 microns. FTIR (Fourier Transform InfraRed) spectrometer obtains an infrared spectrum by first collecting an interferogram of a sample signal using an interferometer, then performs a Fourier Transform on the interferogram to obtain the spectrum. An interferometer is an instrument that uses the technique of superimposing, (interfering)two or more waves, to detect differences between them. The FTIR spectrometer uses a Michelson interferometer. FTIR is an effective analytical instrument for detecting functional groups andcharacterizing covalent bonding information[(4,5)]. FTIR testing identifies chemical compounds in consumer products, paints, polymers,coatings, Pharmaceuticals, foods and other products. Organic molecules are flexible, atoms and groups of atoms can rotate about single covalent bonds. In addition, covalent bonds can stretch and bend as if their atoms werejoined by flexible springs. Infrared spectroscopy, also called IR spectroscopy, probes stretching and bending vibrations of organic molecules.

II. MATERIALS AND METHODS[(7,8)]

Avanafil (Powder form) Casablanca Industrial Private Limited (I n d i a mart – Rajasthan)
Excipients used are Co povidone, Hydroxy Propyl cellulose
Instrumentation- FTIR, UV Visible Spectroscopy

METHOD

The methodology includes 2 steps

1. FTIR spectroscopy
2. Solubility studies

In our project we performed FTIR analysis by pressed pellet technique. In this technique small amount of finely ground solid sample is intimately mixed with about 100 times of its weight of powdered KBr, in a vibrating mill. Finely ground mixture is then pressed under very high pressure (25000p.sig) in evacuable die or minipress to form a small pellet. The resulting pellet is transparent to IR radiation. FTIR analysis is performed for pure drug Avanafil, Avanafil+Co-povidine, Avanafil+Microcrystalline cellulose, Avanafil +HydroxyPropyl cellulose, Avanafil+Mannitol. The peaks were obtained and studied for the alteration of solubility of Avanafil.

PROCEDURE FOR CALIBRATION CURVE OF PURE DRUG

Avanafil is a Class-II drug of BCS classification as it has low solubility and high permeability. Accurately 100mg of pure drug Avanafil was weighed in 100ml of 0.1N HCl. From the above mixture serial dilutions were prepared in concentrations of 1µg, 3 µg,5 µg,7 µg, 9 µg. Absorbance was measured at 236nm in UV spectroscopy. The calibration curve was then plotted against Absorbance V_s Concentration.

SOLUBILITY STUDIES FOR PURE DRUG

Accurately 10mg of pure drug was weighed and mixed with 200ml of water and stirred continuously for about 24 hours and kept aside. The drug mixture was then filtered. The absorbance was measured by UV spectroscopy.

SOLUBILITY STUDIES OF AVANAFIL+MICROCRYSTALLINE CELLULOSE

10mg of pure drug was accurately weighed and mixed with 10mg of Microcrystalline cellulose, 200ml of water was added to it and stirred continuously for about 24 hours and kept aside. The drug mixture was then filtered. The absorbance of the filtrate was measured by UV spectroscopy.

PROCEDURE FOR SOLUBILITY STUDIES OF AVANAFIL + MANNITOL

10mg of pure drug was accurately weighed and mixed with 10mg of Mannitol, 200ml of water was added to it and stirred continuously for about 24 hours and kept aside. The drug mixture was then filtered. The absorbance of the filtrate was measured by UV spectroscopy.

PROCEDURE FOR SOLUBILITY STUDIES OF AVANAFIL + HYDROXYPROPYL CELLULOSE

10mg of pure drug was accurately weighed and mixed with 10mg of Hydroxypropyl cellulose, 200ml of water was added to it and stirred continuously for about 24 hours and kept aside. The drug mixture was then filtered. The absorbance of the filtrate was measured by UV spectroscopy.

PROCEDURE FOR SOLUBILITY STUDIES OF AVANAFIL + CO-POVIDONE

10mg of pure drug was accurately weighed and mixed with 10mg of Hydroxypropyl cellulose, 200ml of water was added to it and stirred continuously for about 24 hours and kept aside. The drug mixture was then filtered. The absorbance of the filtrate was measured by UV spectroscopy.

III. RESULTS AND DISCUSSION

3.1 CALIBRATION CURVE OF AVANAFIL

S. NO	CONCENTRATION(µg /ml)	ABSORBANCE(nm)
1	1	0.098
2	3	0.31
3	5	0.52
4	7	0.72
5	9	0.95

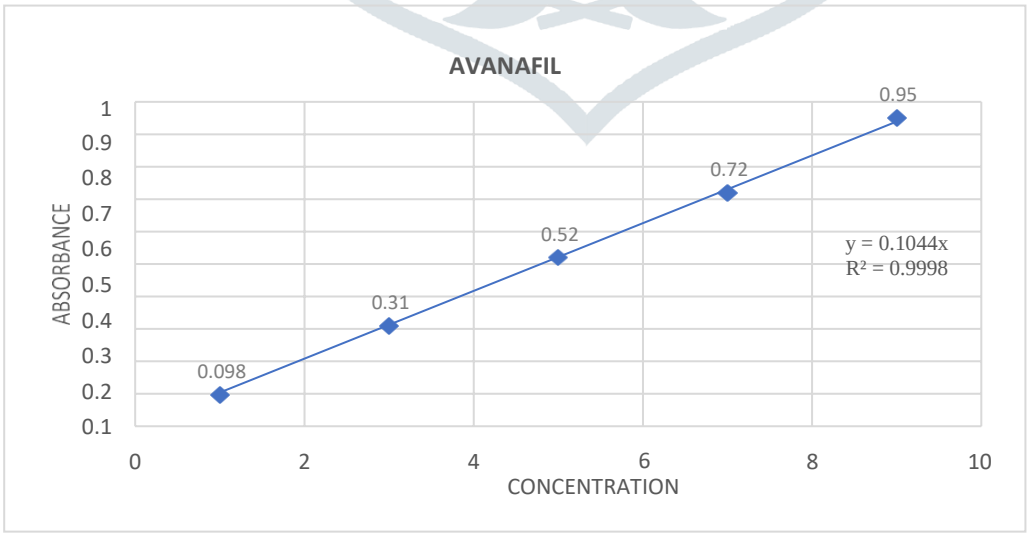

Figure 3.1: Calibration curve of Avanafil

FTIR ANALYSIS

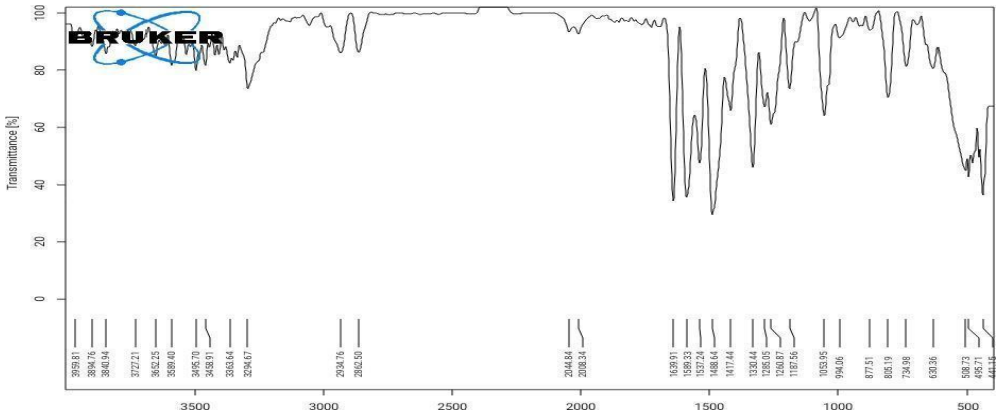

Figure 3.2: FTIR Analysis of Pure drug

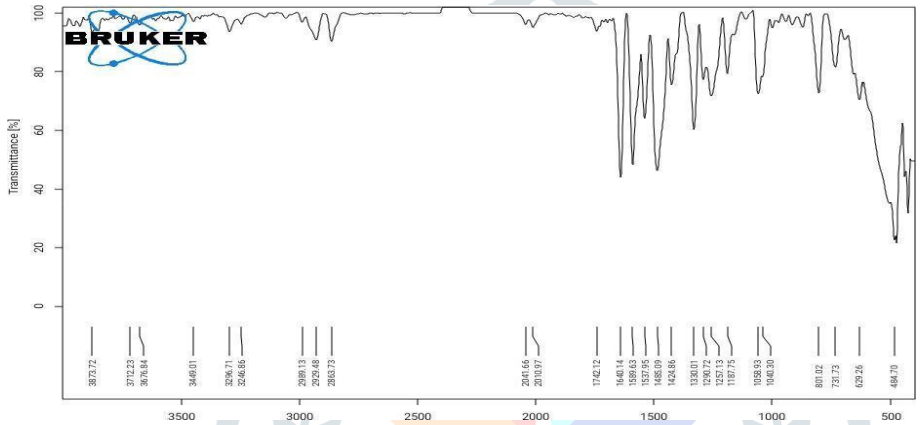

Figure: 3.3 FTIR Analysis of Avanafil with Co-povidone

FTIR ANALYSIS OF AVANAFIL

S.No	Absorption(Cm^{-1})	Group	CompoundClass	Appearance
1.	3652.25	O-H Stretching	Alcohol	Medium, sharp
2.	3589.40	O-H Stretching	Alcohol	Strong, broad
3.	3495.70	N-H Stretching	Primary amine	Medium
4.	3458.91	N-H Stretching	Primary amine	Medium
5.	3363.64	N-H Stretching	Primary amine	Medium
6.	3294.67			
7.	2934.76	N- H stretching	Amine salt	Strong, broad
8.	2862.50	N-H Stretching	Amine salt	Strong, broad
9.	2044.84	N=C=S stretching	Isothiocyanate	Strong
10.	2008.34	N=C=S stretching	Isothiocyanate	Strong
11.	1639.91	C-H bending	Aromatic compound	Weak
12.	1589.33	N-H bending	Amine	Medium

13.	1537.24	N-O stretching	Nitro compound	Strong
14.	1488.64			
15.	1417.44	O-H bending	Alcohol	Medium
16.	1330.44	O-H bending	Alcohol	Medium
17.	1285.05	C-N stretching	Aromatic amine	Strong
18.	1260.87	C-N stretching	Aromatic amine	Strong
19.	1187.56			
21.	994.06	C=C bending	Alkene	Strong
22.	877.51	C-H bending		Strong
23.	734.98	C-H bending		Strong
24.	630.36	C-Br	Halo compound	
25.	508.73	C-I	Halo compound	

TABLE 3.2 FTIR ANALYSIS OF AVANAFIL

FTIR Analysis of Avanafil and Co-Povidone

S.NO	Absorption(Cm^1)	Group	CompoundClass	Appearance
1.	3676.84	O-H	Alcohol	Medium, sharp
2.	3449.01	O-H	Alcohol	Strong, broad
3.	3296.71	O-H	Alcohol	Strong, broad
4.	3246.86	O-H	Alcohol	Strong, broad
5.	2989.13	O-H	Carboxylicacid	Strong, broad
6.	2929.48	O-H	Carboxylicacid	Strong, broad
7.	2863.73	O-H	Carboxylicacid	Strong, broad
8.	2041.66	N=C=S	Isothiocyanate	Strong
9.	2010.97	N=C=S	Isothiocyanate	Strong
10.	1742.12	C-H bending	Aromatic compound	Weak
11.		C= N stretching	Imine/oxime	Medium
12.	1589.63	N-H bending	Amine	Medium
13.	1537.95	N- O stretching	Nitro compound	Strong
14.	1485.09	C- H bending	Alkane	Medium
15.	1424.86	O- H bending	Carboxylicacid	Medium
16.	1330.01	O-H bending	Alcohol	Medium
17.	1290.72	C-N stretching	Aromatic amine	Strong
18.	1257.13	C- O stretching	Aromatic ester	Strong
19.	1187.75	C- N stretching	Amine	Medium
20.	1058.93	C- O stretching	Vinyl ether	Strong
21.	1040.30	S= O stretching	Sulfoxide	Strong

22.	801.02	C- Cl	Halo compound	Strong
23.	731.73	C=C bending	Alkene	Strong
24.	629.26	C-Br stretching	Halo compound	Strong

Table 3.3 FTIR **Analysis of Avanafil and Co-Povidone**

ABSORBANCE OF DIFFERENT EXCIPIENTS WITH PURE DRUG IN WATER

S.No	Excipients	Absorbance(nm)
1.	**Pure drug (10mg) +200ml of water**	**0.386**
2.	**Pure drug + Co-povidone**	**0.932**
3.	**Pure drug + MCC**	**0.531**
4.	**Pure drug + Mannitol**	**0.396**
5.	**Pure drug + HPC**	**0.324**

TABLE 3.4 ABSORBANCE OF DIFFERENT EXPIENTS WITH PURE DRUG IN WATER

IV. CONCLUSIONS:

- Higher Amine groups are insoluble in water. Avanafil contains more number of amine groups which in turn increases the Molar mass of the compound therefore it is low soluble in water.
- Alkynes are more soluble than Alkenes and Alkanes. Avanafil contains alkenes groups though it effects the solubility. The results obtained, indicates that the solubility of class-2 drug Avanafil was enhanced when it is mixed with the excipient Co-Povidone.
- The Co-povidone reacts with Avanafil alters the higher amines in Avanafil which increases the polarity of the drug. Co-povidone also converts the alkenes present in Avanafil which enhances the solubility.

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