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Research Paper

Infrared(IR) Charactizations and physicochemical properties of Schiff base compound obtained by the reaction between 4-Hydroxy-3-methoxy benzaldehyde and 2- Amino-3-methylbutanoic acid

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ABSTRACT
*Some of physicochemical properties of the compound produced from the reaction between **4-** Hydroxy-3-methoxy benzaldehyde and 2- Amino-3-methylbutanoic acid were calculated , the Infrared (IR) spectra was used to charactizations the fundamental bonds of the products obtained from the reaction between the used compounds. The physicochemical properties were calculated according Mol-Soft software, ADME profiling by PreADMET.The results of IR spectra showed presence of some functional groups and bonds relating to the prepared compound. Also some physicochemical properties as (Molecular weight , Solubility , Number of hydrogen bond acceptors , percentage of absorption and number of rotatable bonds were estimated.*

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I. INTRODUCTION

Benzaldehyde (C_6H_5CHO) is an organic compound consisting of benzene ring with a formally substituent , colourless liquid with an odor of almond oil , slightly soluble in water , but it is completely soluble in some organic solvents as ethanol and diethyl ether . benzaldehyde used chiefly in the manufacture of dyes, cinnamic acid and many of organic compounds. Benzaldehyde is prepare by a process in which toluene is treated with chlorine to form benzal chloride followed by addition of benzyl chloride with water. Benzaldehyde was first extracted from bitter almonds in 1803 by the French pharmacist Martrès. In German chemists Friedrich Wohler and Justus von Liebig first synthesized benzaldehyde (Adams *et al* ., 2005).

Benzaldehyde and similar chemicals occur naturally in many foods. Most of the benzaldehyde that people eat is from natural, traditional foods, such as almonds (Adams *et al*., 2005). Almonds, apricots, apples and cherry kernels, contain significant amounts of amygdalin. This glycoside breaks up under enzyme catalysis into benzaldehyde, hydrogen cyanide and two molecules of glucose. Benzaldehyde contributes to the scent of oyster mushrooms (Pleurotus ostreatus) (Beltran *et al*,.1997). It is commonly employed to confer almond flavor to foods and scented products. It is sometimes used in cosmetics products (Andersen, 2006).

In industrial settings, benzaldehyde is used chiefly as a precursor to other organic compounds, ranging from pharmaceuticals to plastic additives. The aniline dye malachite green is prepared from benzaldehyde and dimethylaniline. It is a precursor to certain acridine dyes as well Via aldol condensations, benzaldehyde is converted into derivatives of cinnam aldehyde and styrene. The synthesis of mandelic acid starts from benzaldehyde (Ashurst *et al.*, 2013).

Benzaldehyde reactions:

On oxidation, benzaldehyde is converted into the odorless benzoic acid, which is a common impurity in laboratory samples. Benzyl alcohol can be formed from benzaldehyde by means of hydrogenation. Reaction of benzaldehyde with anhydrous sodium acetate and acetic anhydride yields cinnamic acid, while alcoholic potassium cyanide can be used to catalyze the condensation of benzaldehyde to benzoin. Benzaldehyde undergoes disproportionate upon treatment with concentrated alkali (Cannizzaro reaction): one

molecule of the aldehyde. The aim of this is using some software programmer to estimate the physicochemical properties of the compound obtained by the reaction between 4- Hydroxy-3-methoxy benzaldehyde and 2-Amino-3-methylbutanoic acid (Hindson *et al* ., 2010).

Experimental Part:

Chemical and reagents:

All chemical used in this study were laboratory grade including 4- Hydroxy-3-methoxy benzaldehyde and 2- Amino-3-methylbutanoic acid ,in addition to some solvents and solutions :NaOH, C_2H_5OH, CH_3OH.

Synthesis of Schiff bases:

The Schiff base was prepared as following method : NaOH (20 mmol, 0.8g) was dissolved in methanol (50 cm^3) and 2- Amino-3-methylbutanoic acid (20 mmol) was added. The mixture was stirred magnetically at room temperature , when the mixture became homogeneous,a solution of 4- di methyl amino benzaldehyde (20 mmol, 2.98) in ethanol (50 cm^3) was added After 2 minutes, the solution was evaporated to 20% of it's original volume and 1cm^3 of CH_3COOH was added immediately. After 2 hours yellow crystals appeared. The crystals were filtered and washed with ethanol. They were recrystallized from hot methanol to give yellow crystals .

I.R analysis:

The infrared spectra of the Schiff base was recorded by using the IR (Type Perkin Elymener. FT-IR) spectrophotometer covering the range from 600 to 4000 cm^{-1} , at central lab of Faculty of science, Omar Al-Mukhtar University , Libya.

Physicochemical properties:

The physicochemical properties of compound **(**Schiff base**)** was predicted by Molinspiration, drug-likeness and solubility parameter calculation by Mol-Soft software, ADME profiling by PreADMET .In this regard, Lipinski's rule mainly "drug-like" molecules have logP ≤ 5, molecular weight ≤ 500, number of hydrogen bond acceptors ≤ 10, and number of hydrogen bond donors ≤ 5 (Lipinski *et al*., 1997).

II. RESULTS AND DISCUSSION

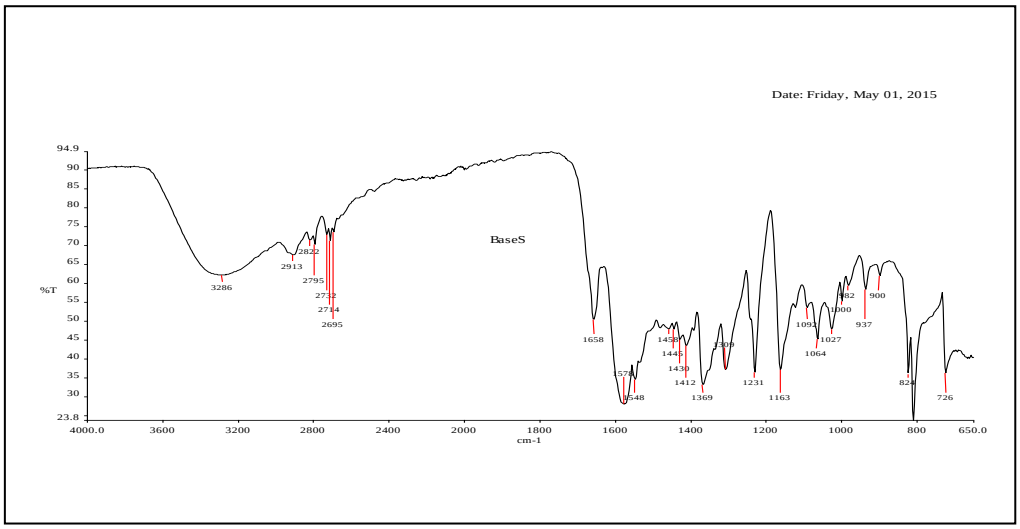
IR spectra studies:-

The (I.R) spectra technique is one of the important methods to study the characterization of the prepare compounds. For comparative purposes and in order to facilitate the spectral assignment of schiff base, the IR spectrum of Schiff base was recorded. The obtained data are presented in ,Table (1) and Figure (1).

Table (1) : The fundamental I.R bands of the Schiff base :

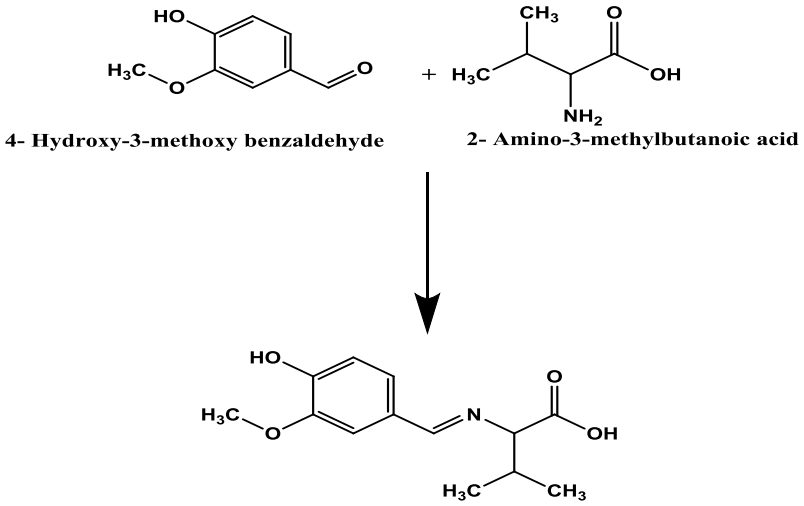
Functional Group	Number wave cm^{-1} Schiff base
OH	3286
CH (Aliphatic)	2882 - 2913
C - O	1231
NH (bending)	1548
CH_2	1430
C-N	1309
CH_3	1369
C=O	1578-1658
C-C	800

The band of Schiff base located at 3286 cm^{-1} are assigned to OH Group (Que et al ., 1999). The bands CH_3, CH_2 and CH (Aliphatic) appear in 1369, 1430 and in the range 2822 - 2913 cm^{-1} respectively:
The NH_2 band appear at 3305 for Schiff base, the NH of the prepared Schiff base band located at 1548cm^{-1} . The C= O band of Schiff base appear in 1571 cm^{-1}. The band C-O which located at 1231 cm^{-1} in Schiff base .The C-C Schiff base band located at 800cm^{-1} , Figure (1).



Figure(1): I-R spectra of the prepared Schiff base

The proposal reaction and the structure of the prepared Schiff base can be in the following reaction:



4- Hydroxy-3-methoxy benzaldehyde **2- Amino-3-methylbutanoic acid**

2-{(4-Hydroxy-3-methoxybenzylidene)amino}-3-methylbutanoic acid

physicochemical properties:

The predicted physicochemical properties of the compound presented in Table **(2)**.The compound under investigation was shown to possess considerable for H-bond donors **2** and H-bond acceptors **5** as shown in Table (2). A poor penetration or absorption is more possible while there are more than **5** H-bond donors, **10** H-bond acceptors. Also, for good membrane permeability clogP value should be **≤ 5**. The test compound had logP **1.77** value. Moreover, we evaluated the compliance of the prepared compound to the Lipinski's 'rule of five' which has been widely used as a filter for substances that could likely be further developed in drug design programs. The results showed that compound obeyed Lipinski's rule of five.

Molecular property prediction is suitable a practical tool in the design of molecules by means of the approved parameters to be helpful drug candidate. Drug design and direct optimization benefits from the capability to expect physical properties such as lipophilicity and solubility, when well as molecular property such as topological polar surface area (TPSA) and number of H-bond donors and acceptors to construct activity prediction means which predicts drug likeness (Cavalla, 2008)

It is significant for conformational changes of molecules under study and ultimately for the required with receptors or channels. It is revealed that for passing oral bioavailability criteria, number of rotatable bond should be **≤10** (Veber, 2002). Tested compound possessed **5** rotatable bonds. Passively absorbed molecules with a TPSA > **140** are consideration to have low oral bioavailability. The tested compound confirmed **TPSA** acceptable value **79.12**. Computed drug-likeness scores are presented in Table **(2)**. Compound having positive values must be measured as drug-like. The tested compound showed drug-likeness scores **-0.67**.

Pharmacokinetic properties play an impart role in the development of successful drug. Pharmacokinetic properties including absorption, distribution, metabolism, excretion, and toxicity (**ADMET**) were calculated using PreADMET. The compound showed high **HIA** values (**90.04 %**) indicating very well- intestinal absorbed compounds. In addition, compound showed medium cell permeability in the **MDCK** cell model with value **352.331 nm/ *sec***. On the other hand, the tested compound was shown to be medium cell permeability in the **Caco-2** cell model with value **20.4299 nm/ *sec* (Table ,3)**. In addition, compound displayed medium **CNS** absorption. Besides, The tested compound was predicted to have weakly plasma protein binding (**81.07%**).

Table (2): physicochemical properties and drug-likeness data of compound(Schiff base).

	Schiff base
cLogP	1.77
MW	251.28
MF	$C_{13}H_{17}NO_4$
HBA	5
HBD	2
Lipinski's violation	0
TPSA	79.12
Volume (A)	234.65
NROTB	5
Drug likeness model score	-0.67
S (mg/L)	**-2.171**

Where:

LogP: logarithm of compound partition coefficient between n-octanol and water.
MW: Molecular weight.
MF: Molecular Formula
HBA: Number of hydrogen bond acceptors.
HBD: Number of hydrogen bond donors.
TPSA: Topological polar surface area.
%ABS: percentage of absorption.
NROTB: number of rotatable bonds.
S: solubility.

Table(2): ADME profiling data of compound.

	Schiff base
[a] **Caco2**	20.4299
[b] **MDCK**	352.331
[c] **HIA**	90.049
[d] **BBB**	0.99
[e] **PPB**	81.077

Where :

[a] **Caco2** (Yazdania ,1998) : Permeability through cells derived from human colon adenocarcinoma; Caco2 values < 4 nm/*sec* (low permeability), values from 4 to 70 nm/ *sec* (medium permeability) and values > 70 nm/*sec* (high permeability).

[b] **MDCK** (Irvine *et al.,* 1999): Permeability through Madin–Darby canine kidney cells; MDCK values < 25 nm/*sec* (low permeability), values from 25 to 500 nm/*sec* (medium permeability) and values > 500 nm/*sec* (high permeability).

[c] **HIA:** Percentage human intestinal absorption; HIA values from 0 to 20% (poorly absorbed), values from 20 to 70% (moderately absorbed) and values from 70 to 100% (well absorbed).

[d] **BBB:** Blood–brain barrier penetration; BBB values < 0.1 (low CNS penetration), values from 0.1 to 2 (medium CNS absorption) and values > 2 (high CNS absorption)
[e] **PPB:** Plasma protein binding; PPB values < 90% (poorly bound) and > 90% (strongly bound).

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