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Research Article

Physiochemical Evaluation of Bisoprolol Gel 1%

Abdel Rasool.A.M [1], Tawfiq.N.O.M[2], Ayoub.R.S [3]

[1]College of dentistry, University of Mosul, Iraq.

[2]College of medicine- Neineva, University of Neineva, Iraq.

ABSTRACT

Objective: This study aimed to evaluate the physiochemical properties of Bisoprolol fumarate Gel 1% and drug excipient interaction by different methods

Methods: Bisoprolol fumarate gel was prepared by mixing (0.005,0.01, 0.02) gm of Bisoprolol fumarate powder in 100ml gel base to give a final concentration of (0.5%, 1%, 2%) to prepare a homogeneous gel. Depending on pilot study result, Bisoprolol fumarate gel 1% was chosen to be studied. Some of the physical characters (melting point, density and pH) of the prepared formulae were evaluated. Drug excipient interaction was evaluated also by infrared spectroscopy, UV -visible spectrophotometer and HPLC methods.

Result: The prepared bisoprolol gel 1% was homogenous with a melting point of 98C^0, a density of 1.05 gm/ml, Determination of bisoprolol gel 1%pH was7.48pH while the pH of the gel alone was 7.6 , viscosity of bisoprolol fumarate gel was(175.314866), The result of drug excipients interaction using infrared red and the ultraviolet spectra and HPLC revealed no chemical interaction between bisoprolol power and gel used in the present study.

Conclusion: The results revealed that bisoprolol fumarate powder used was pure and that no interaction between drug and excipient.

Key words: Bisoprolol gel, melting point, Infrared spectroscopy, UV -visible spectrophotometer, HPLC.

INTRODUCTION

Bisoprolol is a cardioselective β-blocker without membrane stabilizing activity or intrinsic sympathomimetic activity pharmacokintic action competitively blocks β1-adrenergic receptor. The molecular weight is 383.48; the white crystalline substance, melts at 101°C. Bisoprolol fumarate is very freely soluble in water and methanol and freely soluble in ethanol and chloroform.

Chemically it is (±)-1-[4-[[2-(1-methylethoxy) ethoxy] methyl] phenoxyl-3-[(1-methyl ethyl) amino]-2-propanol. It possesses an asymmetric carbon atom in its structure and is provided as a racemic mixture [1].

Bisoprolol is a cardioselective β-blocker without membrane stabilizing activity or intrinsic sympathomimetic activity pharmacokinetics action competitively blocks *β1*-adrenergic receptor. [2] Bisoprolol have greater affinity for *β1* than for *β2* receptors these are examples of *β1*-selective antagonists there was highly selectivity [3]. The preparation of the Bisoprolol fumarate gel 1% ,determination, the Physical evaluation of bisoprolol fumarate gel 1% of (melting point, density, pH) and drug excipient interaction (infrared spectrophotometer, (UV-visible spectrophotometer) and HPLC high pressure liquid chromatography were carried out in this study.

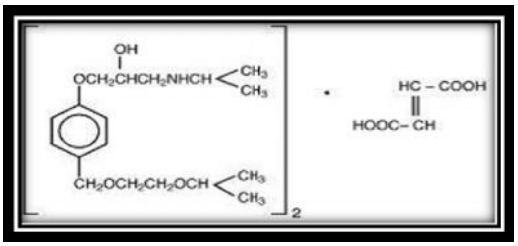

Figure 1: Chemical structure of Bisoprolol fumarate

MATERIAL AND METHOD

Bisoprolol fumarate powder was used in this study (w.s name Bisoprolol fumarate) (ID No.; WS/11/019/01) Purity; 101.3% Q.C No R11683 W.C % 0%ofthe united company (Jordan manufacture)

Preparation Bisoprolol fumarate Gel: Bisoprolol fumarate gel was prepared by mixing (0.005 ,0.01, 0.02) gm of Bisoprolol fumarate powder in 100ml gel base to give a final concentration of (o. 5%, 1%, 2%) as table (1) with continuous mixing using vortex device to prepare a homogeneous gel, Gel was kept in plastic containers and store at room temperature [4], and then applied to pilot study rabbit using these three conservation and the two concentrations is excluded from the study 2 % and 0.5%.

Physiochemical evaluation of bisoprolol gels1%

Measurement of melting point of bisoprolol fumarate: The measurement was carried out by using (electrothermal melting point apparatus Stuart UK) the measurement is carried out in a Mosul university college of Science department of chemistry. [4.]

Determination of density of the gel density

The determination of gel density was done by weight the volumetric flask without gel and weight of volumetric flask with gel

The determination of the density of the bisoprolol fumarate gel was done by measuring its mass per unit volume, in the metric system, density has units of kg/L or gm /ml [5]. The density was measured by using the following formula:

$$D = W_2 - W_1 / V$$

Where D: density of sample.

W_1: weight of volumetric flask when empty.

W_2: weight of volumetric flask when full.

V: volume of volumetric flask.

Determination of Gel pH: The pH of bisoprolol fumarate gel was determined by putting the electrode of pH meter inside the tube which contains few milliliters of the tested samples. The determination of pH value in was done bisoprolol fumarate gel and The determination of vehicle gel.[6]

Determination of viscosity bisoprolol Gel : the viscosity of bisoprolol fumarate gel measurement was carried out by Put the gel in viscometer and then calculate the time of the descent of the gel in the device at room temperature, Determination of viscosity of bisoprolol fumarate gel was done by using Ostwald viscometer which is a simple device and accurate for measuring the viscosity of liquid, usually the viscosity of the liquid is determined by comparison with a standard such as water by using the following formula: [7]

$$n_1/n_2 = p_1t_1/p_2t_2$$

p_1: density of distilled water.

t_1: time to pass the distilled water in seconds.

p_2: density of sample.

n_2: viscosity of distilled water

t_2: time to pass the bisoprolol fumarate gel in seconds

The viscosity was measured on freshly prepared samples, just after the end of stirring process

Drug excipient' s interaction

The technique in this study IR spectroscopy was employed. IR spectroscopy is one of the most powerful analytical techniques which offer the possibility of chemical identification [8]. The Bisoprolol fumarate powder, gel base carboxy methylcellose and bisoprolol fumarate gel 1% and its blend with occupants were scanned and recorded in the range of (600-3900) cm^{-1}, by using Infrared spectrophotometer (FTIR-600) carried out in a Mosul university college of science, department of chemistry Re taking the IR in the central laboratory in the College of Agriculture and Forestry University of Mosul (ALPHA) [9].

UV -VISIBLE spectrophotometer was examined by using instrument (SHIMADZU UV1650PC) (wave length 190.0-1100.0) (Japan) the measurement is carried out by using the deionized water as solvent with (1cm) diameter quartz cell by using of bisoprolol fumarate powder and gel alone and bisoprolol fumarate gel carried out in Mosul university college of science department of chemistry [9].

HPLC method for determination of bisoprolol in presence of gel

The stock solution of bisoprolol fumarte gel , Bisoprolol fumarte poweder and gel was prepared by dissolved with suitable solvent(deionized water) and is filter by filter paper, HPLC procedure was proposed using C18 column GL science 4-6 *250mm and the mobile phase consisted of acetonitrile and 0.01M phosphate buffer(pH7.4) at ratio (30:70 v/v) and the absorbance of prepared solutions was measured at max 228nm at temperature $37C^0$ and injected volume was 20microlitter of each solution at flow rate 1ml /min was examined in Ministry of industry and minerals in Al-Kindy state company[10] .

RESULT

Physical evaluation of bisoprolol fumarate gel

Measurement of melting point:

Melting point of bisoprolol fumarate powder is 98 C^0 from the result of melting point of bisoprolol fumarate powder that indicated a pure bisoprolol fumarte was used

Determination of density of the bisoprolol fumarate gel:

The Density of bisoprolol fumarte gel 1% was measured and the results are (1.05) g/ml

Determination of viscosity bisoprolol fumarate gel:

The descent time of the bisoprolol fumarte gel1% in the Viscometer is 1497sec at $20C^0$ is (175.314866)

Determination of bisoprolol fumarate gel 1% pH

Evaluation of the gel alone is (7.48) bisoprolol fumarte gel 1% pH of was done

Determination of viscosity bisoprolol fumarate gel

The descent time of the bisoprolol fumarte gel1% in the Viscometer is 1497sec at $20C^0$ was (175.314866)

Drug excipient' s interaction

Infrared red and The ultraviolet spectra revealed in the absence of possible chemical or physical interaction between both drug and excipient in the present study the gel (carboxy methy cellos and propylene glycol) and only a carrier for the pure bisoprolol format and no chemical interaction.as (figure 2) and(figure 3)

HPLC method for determination of Bisoprolol gel

HPLC separation method explain there was no interference between both drug and excipient as(figure 4)

DISCUSSION

Topical delivery of drug products may offer advantages, increased compliance, avoidance of first pass metabolism by the liver, delivery of a more even level of the therapeutic agent over time, and the possibility of reduced side effect[11]. The melting range of a pure solid organic is the temperature range at which the solid is in equilibrium with its liquid. As heat is added to a solid, the solid eventually changes to a liquid. Taking the melting range of a sample is useful for two reasons, Identification of an unknown sample Its observed melting range with that of known substance comparing an observed range for an actual sample of the known range for a pure sample, you can tell whether your actual sample is pure or contaminated (the range is depressed and broadened)[12]. The ultraviolet-visible reference spectra presented here were obtained by the use of double beam spectrophotometers with sample solutions prepared as specified in the individual monographs. The horizontal axis indicates the wavelength (NM) and the vertical axis indicates the absorbance Spectroscopy is a technique that measures the interaction of molecules with electromagnetic radiation. Light in the Near-ultraviolet (UV) and visible range of the Electromagnetic spectrum has an energy of about 150–400 kj Mol^{-1}The energy of the light is used to promote electrons from the ground state to an excited state, Absorption spectroscopy is therefore anExcellent technique for following ligand-binding reactions, Spectroscopic measurements are very sensitive and nondestructive, and require only small amounts of material for analysis [13]. In this study there was no interaction between drug and exicipent, High performance layer chromatography The results of the analysis of pharmaceutical dosage forms by the proposed HPLC method are highly reliable and are in good agreement with the labeled claim of the drug. The percent indicates non interference from the most common accidents in the gel formulations. The proposed HPLC method is found to be simple, sensitive, accurate, precise, specific And robust can be used for the routine simultaneous estimation of Bisoprolol fumarate gel in the new pharmaceutical dosage form [14].

As seen in figure-2, FTIR IR spectrophotometry Drug-Excipient compatibility study data, significant changes in peak positions were not observed between pure drugs, mixture of drug and excipients thus indicating no chemical interaction between drug and excipients. So it is clear Bisoprolol fumarate is compatible with all the accidents tested above [8].

Table 1
Composition of three concentrations of Bisoprolol gel (0.5%, 1%, 2%)

Ingredient	B1	B2	B3
Bisoprololfumarate powder (gm)	0.005	0.01	0.02
Gel base (carboxy methycellose and propylene glycol)(gm)	1	1	1

The **B1** was Bisoprolol fumarate 0.5%, **B2** Bisoprolol fumarate1%, **B3** Bisoprolol fumarate2%

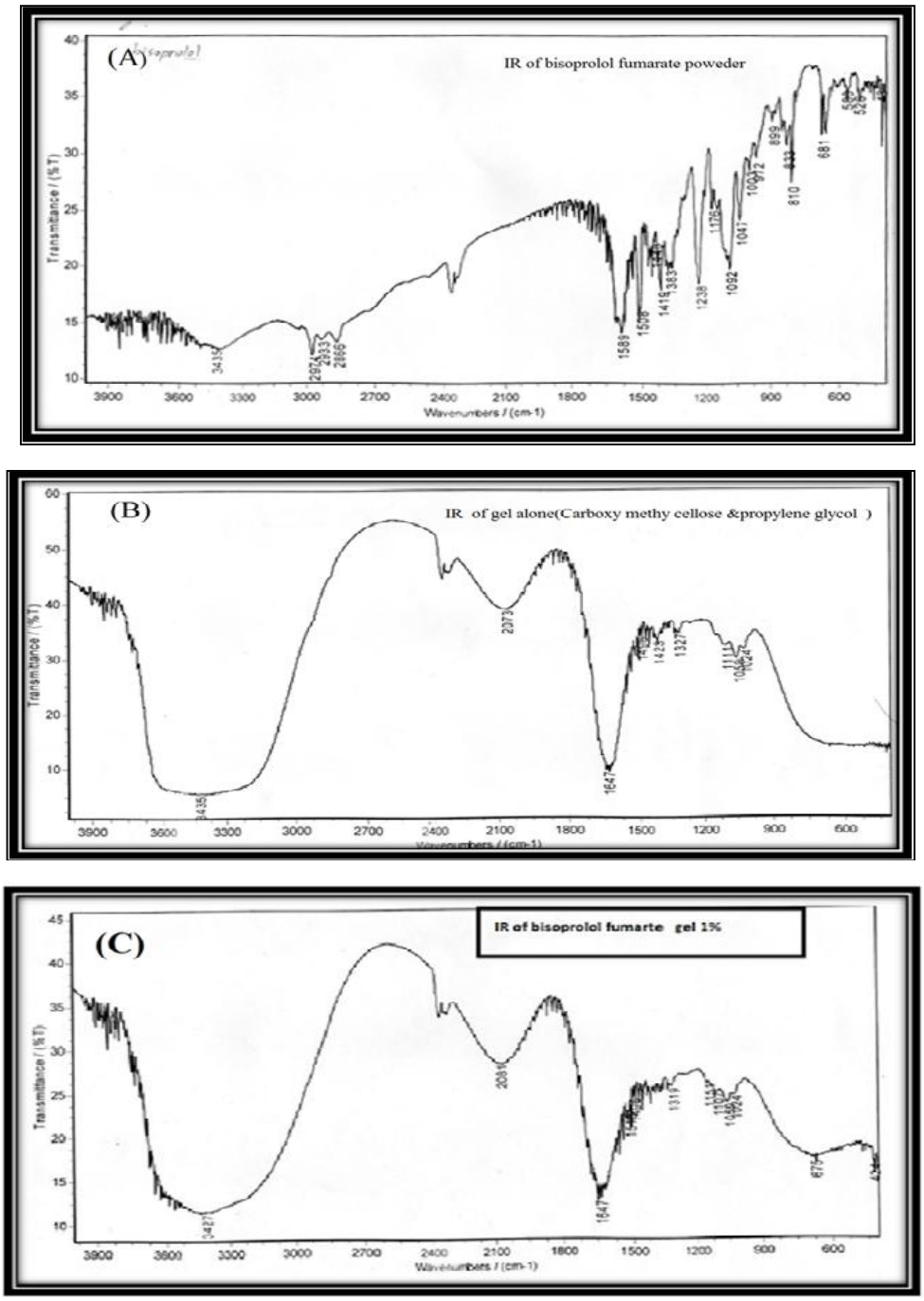

Figure 2
(A) IR spectrophotometry of bisoprolol powder (B) IR spectrophotometry of gel alone (CMC&PG) (C) IR spectrophotometry of bisoprolol fumarate gel 1%

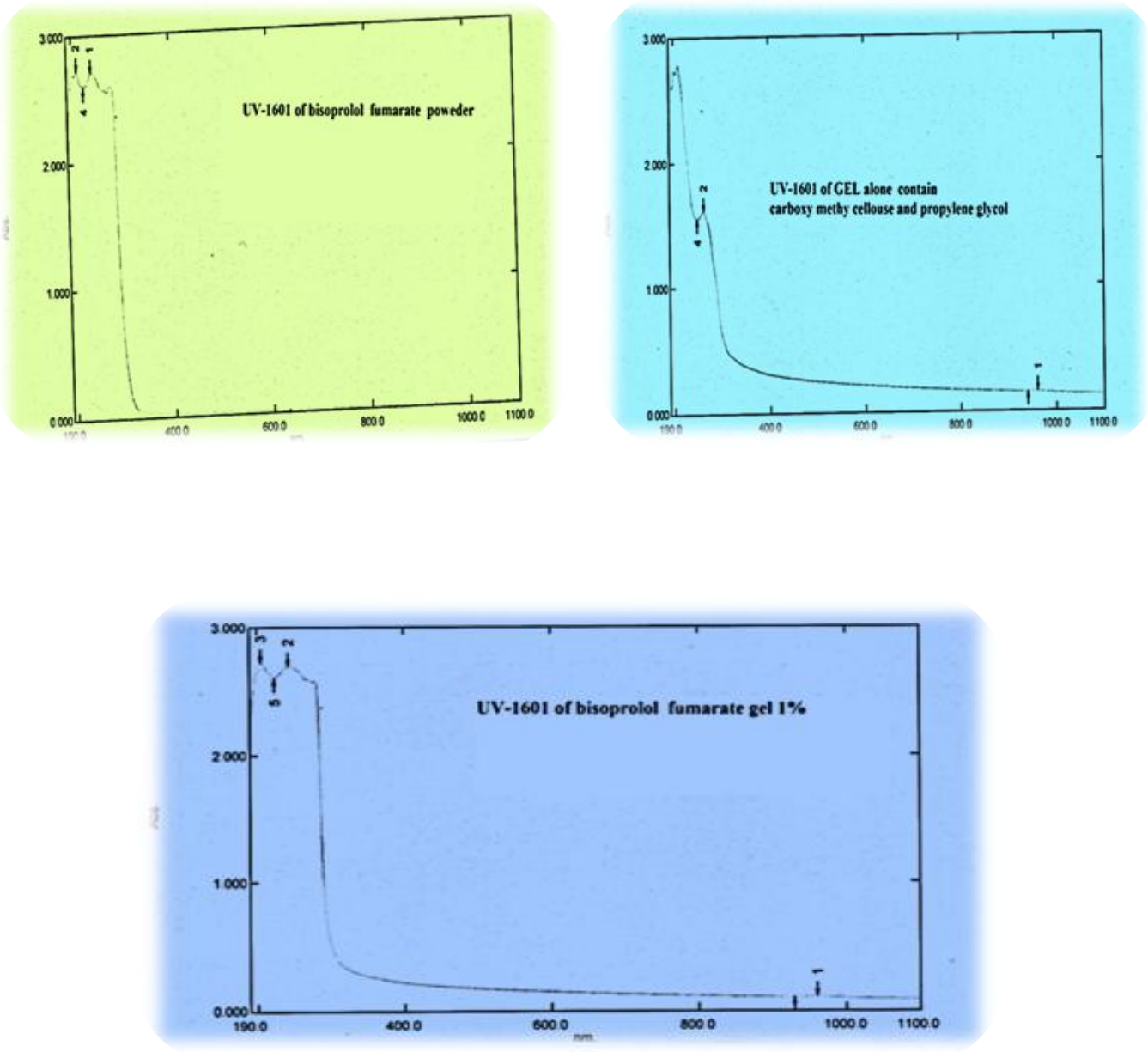

Figure 3
UV 1601 (A) bisoprolol fumarate powder (B) GEL alone carboxy meticulous and propylene glycol (C) bisoprolol fumarate gel 1%.

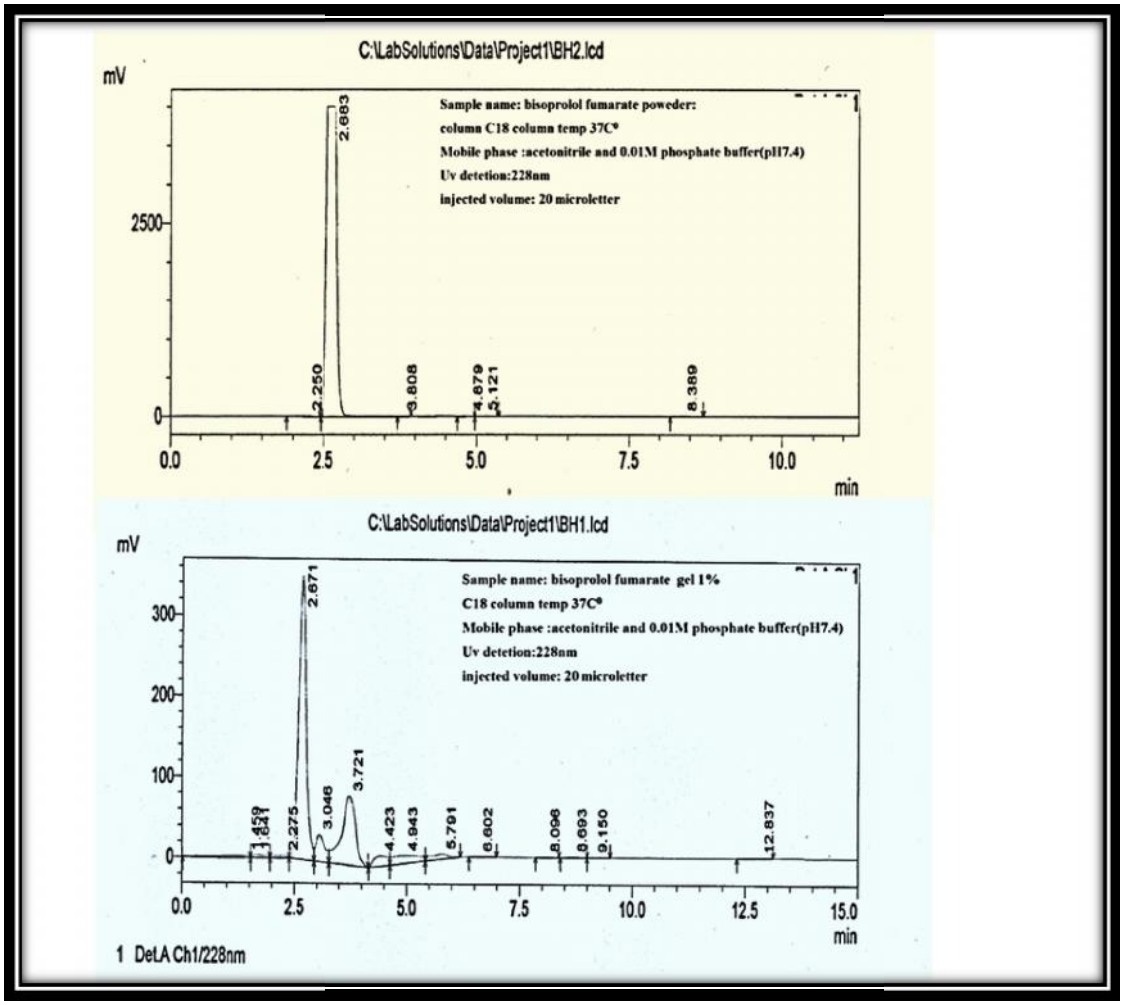

Figure 4
HPLC of bisoprolol fumarate powder above and HPLC bisoprolol gel 1%below

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