Determination of Free Chemical Potential for Finasteride Diffusion through SDS Micelle Suggested as Alternative Living Membrane System

Oraas Adnan Hatem[1,*] and Ahmed Jassim Obaid[2]

[1,2]*University of AL-Qadisiyah, College of Science, Department of Chemistry, Iraq*

Abstract: As an alternative living cell membrane, sodium dodecyl sulfide (SDS) has been investigated at this study, spectroscopic assessment of Finasteride diffusion through the alternate model of the cell membrane in two distinct polar solutions, buffer phosphate solution pH 7.4 and Cyclohexane(Non-polar solution), has been studied. Finasteride in buffer phosphate solution showed a definite λ_{max} at 253 nm, which was consistent with the default values. The results also reveal that the non-polar medium has a lower attenuation coefficient and a shorter maximum wavelength than the polar medium. The pH 7.4 finasteride solution demonstrated remarkable stability over time.

Diffusion rate of Finasteride was investigated using Sodium Dodecyl Sulfate (SDS) as an alternative cell membrane model. The chemical potential was determined to be - 6294.76 J mol^{-1}, showing the spontaneity of the compound's diffusion process.

The results indicated that Finasteride may diffuse (at a rate constant of 51.11 min^{-1}) from the aqueous media and other identified components to the inner micelle; the equilibrium constant for diffusion was calculated to be 11.5.

Keywords: Finasteride, Diffusion, Chemical potential, SDS, Alternative model, Cell membrane.

INTRODUCTION

Benign prostatic hyperplasia BPH is a noncancerous, androgen-independent growth of the periurethral prostate gland that causes urinary blockage [1]. The most frequent cancer in men is prostate cancer over the age of 50, and it becomes more common as they age. It is also the biggest cancer's cause mortality [1, 2].

Finasteride (4-azasteroid) (FIN), is an efficient 5-alpha-reductase inhibitor, the enzyme that transforms testosterone into androgen dihydrotestosterone (DHT) [3] Figure **1**. Increased DHT levels maintain growth in prostate cancer and BPH progression [4].

FIN is useful in preventing prostate cancer [5] due to its rapid absorption and extensive distribution in the body following oral intake. As a result, it is vital to develop a sensitive and precise assay for FIN in pharmaceutical bulk medications and human biofluids. HPLC [6-8], isotope-dilution mass spectrometry [9], polarography [10], spectrophotometer [11], and high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) [12] have all been used to quantify FIN in biological materials.

SDS, often known as lauryl sulfate is an alcohol sulfate detergents compound. It's also suggested to be an ionic detergent that helps biological membranes burst quickly [13]. It is composed of a twelve carbon series linked to a sulfate group. This group is a sulfuric acid and dodecyl alcohol ester, as well as dodecyl hydrogen sulfate sodium salt

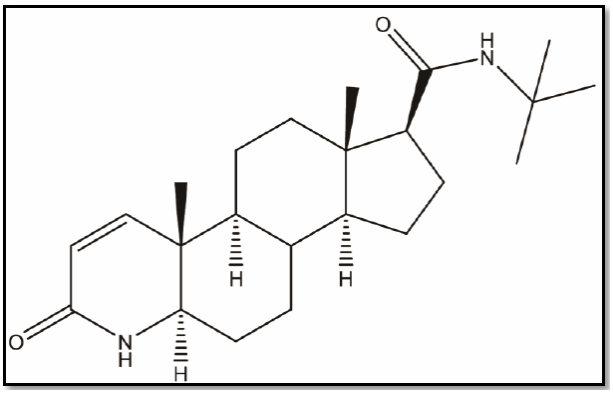

Figure 1: Finasteride's chemical structure.

The amphiphilic features of SDS are provided by the hydrocarbon tail and the polar "head group," which require to be used as a detergent [14, 15]. Micelles are amphiphilic surfactant molecules that form spherical vesicles when they come into contact with an aqueous solution [16].

In many detergent applications, interactions between synthetic polymers and surfactant molecules in aqueous environments remaining crucial, as well as the chemical, pharmaceutical, health care, and

*Address correspondence to this author at the University of AL-Qadisiyah, College of Science, Department of Chemistry, Iraq;

E-mail: oraas.adnan@qu.edu.iq; ch.post10@qu.edu.iq

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petroleum sectors. Surfactant molecules and polymers, in general, alter the rheological features of solutions, features include colloidal dispersion stability, adsorption properties at solid-liquid interfaces, liquid-liquid interfacial tensions, and the capacity of sparingly soluble molecules to be dissolved in water.

Micellar solubilization is an important feature of surfactant solutions that is extensively exploited in pharmaceutical formulations, notably to boost drug bioavailability [17].

EXPERIMENTAL

Aqueous buffer phosphate solutions were produced by combining a certain volume of Potassium di hydrogen phosphate with a concentration of 0.0667 M. Following pH adjustment, the volume was completed with Sodium phosphate dibasic dehydrate at a concentration of 0.0667M to 100mL. As a stock solution, aqueous solutions of Finasteride with a concentration of 2.6 $x10^{-4}$ M were prepared.

Spectroscopic analysis were performed in the range of 200-400 nm using a Shimadzu 1800 UV-spectrometer at 37°C for drug solution, Cyclohexane, and drug solution in SDS micelle (concerning CMC in the production process).

RESULTS AND DISCUSSION

Spectroscopic Study of Finasteride

Finasteride (2.6 $x10^{-4}$ M) spectroscopic characteristics were studied in various polarity media at 37 C^{o} (Figure **2**). When the solution shifted from polar to non-polar, there was a blue shift and hypochromic impact, with a maximum wavelength of 253 nm in the buffer phosphate solution, in agreement with earlier research [18, 19]. In Cyclohexane, λmax was equivalent to 248 nm (Table **1**).

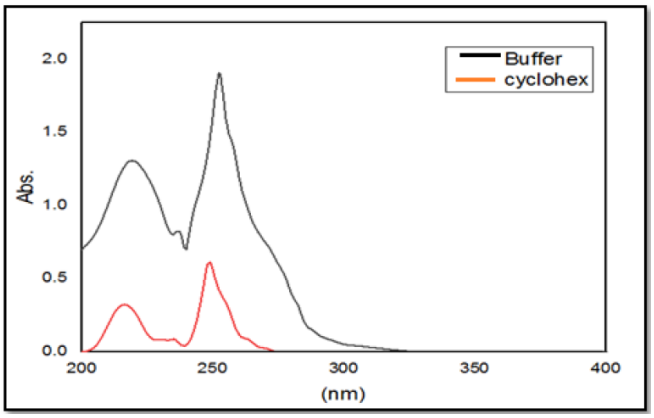

Figure 2: UV spectrum of Finasteride 2.6×10^{-4} M in cyclohexane and pH 7.4 buffer phosphate.

Table 1: Molar Attenuation Coefficient of Finasteride in Cyclohexane and pH 7.4 Buffer Phosphate

Wavelength /nm	Attenuation coefficient/1/mol .L/cm	
	Buffer Phosphate	Cyclohexane
248.00	5192.31	2307.69
249.65	5807.69	2192.31
250.06	6269.23	2076.92
250.84	6692.31	1923.08
251.20	6769.23	1846.15
251.61	7153.85	1807.69
251.98	7230.77	1692.31
252.30	7269.23	1615.38
253.00	7307.69	1538.46
253.53	6923.08	1461.54
254.30	6538.46	1346.15
255.08	6076.92	1269.23
256.22	5615.38	1076.92
258.50	5115.38	653.85

The phenomena of solvatochromism was discovered in the action of pharmacological solutions; the name solvatochromism is employed to describe the claimed shift in wave length and absorbance of a UV-visible absorption band owing to a change in medium polarity. When absorption spectrum in various polarity solutions were studied, it was observed that the type of the solvent affected not only the wave length of the absorption peak but also its intensity and, in some cases, its shape [20].

A change in molecule geometry can explain the hypsochromic shift of the wave length in Cyclohexane drug solution due to decreasing the energy level position of π MO by the solvent effect. A noteworthy feature that adds to the explanation is the difference in solvent dielectric constants (it is 2.02 $F \cdot m^{-1}$ for cyclo hexane compared to 80 F/m for water), as well as the gap between the ground and excited states of the solvent-solute interaction.

The intensity of the absorbance peak increased with medium polarity, where the polarity of excited state π* increases by polar solvent. As a result, the value of the attenuation coefficient goes up [21, 22].

The leading causes of the spectrum shifts were particular solute-solute and solute-solvent interactions and bulk solvent characteristics. The sensitivity to the solvent polarity could be used to understand spectrum shifts in systems without an intermolecular hydrogen bond. As a result, raising the polarity of the solvent causes a bathochromic shifting of the bands (π-π*) in many molecules [20, 23].

Finasteride Diffusion through SDS Micelle Solutions

The chemical potential was calculated after investigating the rate of medicinal compound diffusion across SDS micelles with a concentration of 0.2×10^{-2} M. Finasteride's absorbance has shown to change significantly over time (Figure **3**, **4**). (Tables **2**, **3**)

The calculations were performed at a λ_{max} = 253 nm:

$$C_{aq\ out\ side\ micelle} \overset{K_{eq}}{\Leftrightarrow} C_{org\ in\ side\ micelle}$$

$$A_{totla} = A_{aq} + A_{org} \quad (1)$$

$$\therefore A_{totla} = \varepsilon_{aq} C_{aq} + \varepsilon_{org}\left[C_{initial} - C_{aq}\right] \quad (2)$$

where:

Atot: Finasteride total absorbance

Aaq: Finasteride absorbance in aquaouse solution

Aorg: Finasteride absorbance in organic solution

ε_{aq}: Extension coefficient of Finasteride in aqueous solution

ε_{org}: Is the extension coefficient of Finasteride in organic solution

$C_{initial}$: Finasteride initial concentration

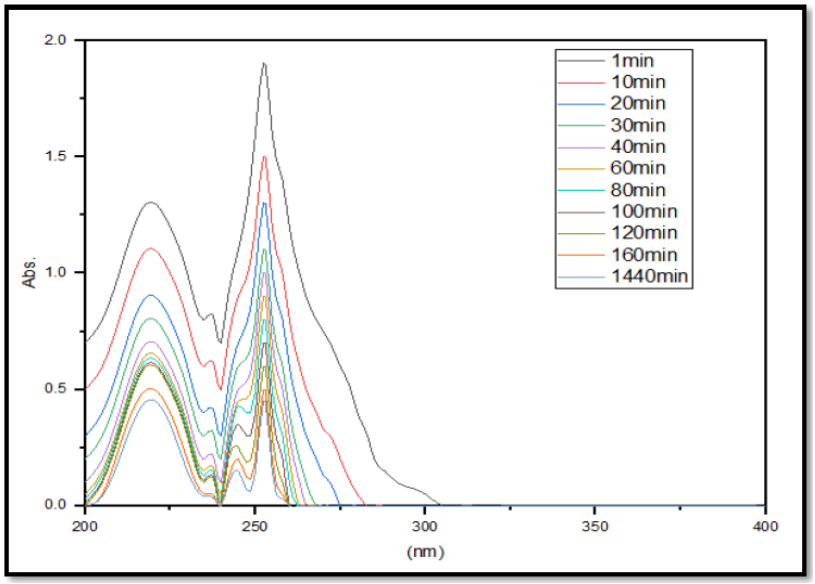

Figure 3: Decreasing the absorption of Finasteride with time as a result of diffusion through SDS.

Table 2: Finasteride Diffusion Behaviour with Time

Wavelength/ nm	Time/min										
	1	**10**	**20**	**30**	**40**	**60**	**80**	**100**	**120**	**160**	1440
248.00	1.35	1.01	0.81	0.68	0.55	0.42	0.30	0.19	0.12	0.11	0.10
249.65	1.60	1.14	0.99	0.74	0.63	0.58	0.51	0.32	0.20	0.16	0.15
250.06	1.63	1.19	1.00	0.81	0.68	0.59	0.52	0.37	0.29	0.22	0.21
250.84	1.71	1.32	1.13	0.93	0.82	0.81	0.67	0.52	0.41	0.32	0.30
251.20	1.80	1.39	1.18	0.97	0.88	0.84	0.69	0.56	0. 48	0.38	0.37
251.61	1.83	1.41	1.22	1.01	0.92	0.85	0.71	0.62	0.53	0.41	0.39
251.98	1.85	1.46	1.26	1.07	0.96	0.86	0.77	0.66	0.56	0.45	0.43
252.30	1.87	1.48	1.29	1.10	1.00	0.89	0.79	0.69	0.59	0.48	0.46
253.00	1.9	1.52	1.34	1.14	1.05	0.93	0.82	0.79	0.63	0.52	0.50
253.53	1.82	1.43	1.24	1.05	0.94	0.85	0.74	0.65	0.54	0.44	0.43
254.30	1.68	1.32	1.14	0.93	0.82	0.73	0.62	0.53	0.42	0.33	0.33
255.08	1.59	1.19	1.01	0.81	0.71	0.60	0.50	0.41	0.31	0.20	0.20
256.22	1.47	1.09	0.90	0.71	0.59	0.49	0.33	0.26	0.19	0.09	0.09
258.50	1.36	0.84	0.75	0.56	0.45	0.37	0.25	0.14	0.07	0.05	0.04

Table 3: Finasteride Concentration in Buffer Phosphate and Cyclohexane with Time at λ_{max}

Time/min	$C_{aq}/10^{-4}$M	$C_{org}/10^{-4}$ M	Xe/(Xe-X)	Ln [Xe/(Xe-X)]
1	2.60	0.00	1.00	0.00
10	1.94	0.66	1.38	0.32
20	1.63	0.97	1.68	0.52
30	1.28	1.32	2.23	0.80
40	1.13	1.47	2.60	0.96
60	0.92	1.68	3.37	1.21
80	0.73	1.87	4.60	1.53
100	0.68	1.92	5.11	1.63
120	0.40	2.20	12.55	2.53
160	0.21	2.39	-	-

C_{aq}: Finasteride concentration in aqueous solution

From Table **1**:

$$A_{totla} = 7307.69\ C_{aq} + 1538.46\left[C_{initial} - C_{aq}\right] \quad (3)$$

Use initial concentration and rearrangement of the equation:

$$A_{totla} - 0.4 = 5769.23\ C_{aq} \quad (4)$$

From the equation of first order reversible reaction:

$$t = \frac{1}{k_1 + k_{-1}} In \frac{xe}{xe - x} \quad (5)$$

$$K_{eq} = \frac{Xe}{a - Xe} \quad (6)$$

$$K_{eq} = \frac{K_1}{K_{-1}} \quad (7)$$

Where:

X: Finasteride concentration in n-Hexane at time t

Xe: Finasteride concentration in cyclohexane at equilibrium

plutting $In \frac{Xe}{Xe - X}$ aganist time give a straight line with a slope of $(k_1 + k_{-1})$ Figure **4**:

$Slop$ = 0.018

$$\therefore \frac{1}{k_1 + k_{-1}} = 0.018$$

$$\therefore K_1 + K_{-1} = 55.56$$

$$\frac{K_1}{K_{-1}} = 11.5$$

$K_1 = 51.11\ min^{-1}$

$K_{-1} = 4.45\ min^{-1}$

$$t_{0.5} = \frac{0.693}{k_1 + k_{-1}} \quad (8)$$

So: $t_{0.5} = 0.0124$ min

$$\Delta G^{\circ} = -RT\ Ln\ K_{eq} \quad (9)$$

$$\Delta G^{\circ} = -6294.76\ J\ mol^{-1}$$

Finasteride diffusion via SDS micelle is a spontaneous process, as demonstrated by the negative Gibbs free energy value (chemical potential). Finasteride absorbance in SDS decreases, indicating that Finasteride is entering the organic medium within the micelle from the aqueous solution outside the micelle. It is worth noting that there was no interaction between Finasteride and the buffer phosphate employed as a solvent in the SDS solution preparation.

The complete absence of any reaction between the buffer phosphate component and Finasteride, as well as the low value of Finasteride's attenuation coefficient in organic non-polar solvents compared to the high value in aqueous media, and the drop in Finasteride absorbance in SDS solution, all indicate that Finasteride enters the organic media from the aqueous solution outside the micelle.

CONCLUSION

The presented results are promising and constitute a basis for the development of a simple and generic strategy for the fabrication of alternative living cell membranes for the *in vitro* study of pharmacokinetics

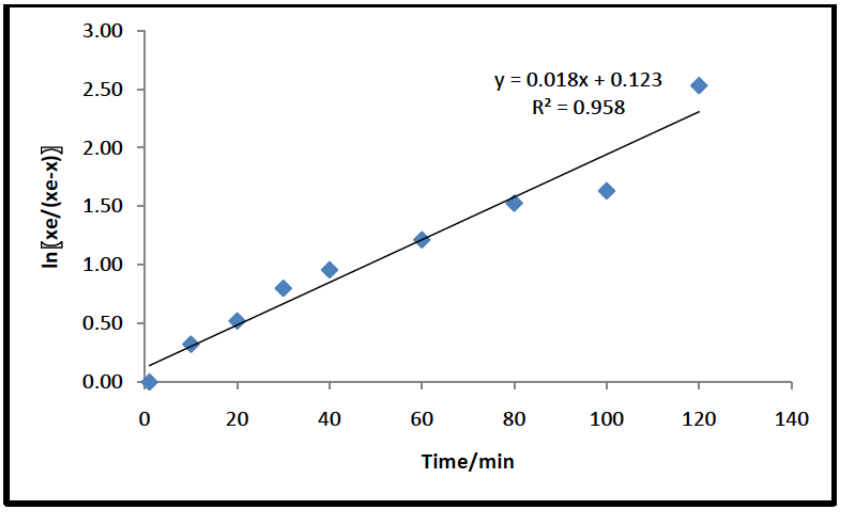

Figure 4: Reversible first-order relation of Finasteride diffusion through Sodium dodecyl sulfate.

properties of new pharmaceutical compounds such as the diffusion rate that investigated in this study.

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