

## Impact of Ionic Strength on the Solubility, Density, Viscosity, and Conductivity of Aspirin in Aqueous Phase

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### ABSTRACT

ASA is an odorless, colorless to white, crystalline powder with the chemical formula  $C_9H_8O_4$ [12]. It is a phenolic acid compound, is a metabolite of salicin, one of the oldest pain relievers derived from willow bark. At the same time, it is a precursor of a well-known drug, ASA is widely used as an intermediate for the production of many industrial compounds. In this sense, salicylic acid is one of the active ingredients in cosmetic products. The present paper reveals the impact of various salts on the physicochemical properties of Aspirin (Acetylsalicylic Acid)(ASA) in aqueous solutions. The study evaluates how the addition of sodium chloride, calcium chloride magnesium chloride, and iron (III) chloride influences the solubility, density, viscosity, and degree of dissociation of ASA in aqueous solutions. These insights are crucial for optimizing pharmaceutical formulations and improving drug delivery efficiency in therapeutic applications.

### I. INTRODUCTION

Pharmaceuticals are probably the most important chemical substances in use in the everyday life [1]. Among various drug delivery systems, oral drug delivery is the most common, convenient, safer and favored route due to the low cost of drug treatment and patient compliance. Oral drug absorption is governed by factors viz. solubility, dissolution and permeability and their enhancement, it is one of the most challenging aspects of drug delivery system[2]. Many pharmaceutical drugs are poorly water-soluble, and this property hinders their ability to reach the systemic circulation in the required concentration for optimal therapeutic effect. To overcome this problem, such drugs can be formulated with different salts [3], their physicochemical properties can be easily tuned by appropriate selection of the cation and the anion or an introduction of

substituents with the molecule of cation or anion. Therefore, in the last few decades, they have attracted great interest due to their potential diverse applications [4]. Salts of acidic and basic drugs have higher solubilities as compose with the corresponding acid or base forms. Salt formation to increase aqueous solubility is the most preferred approach for the development of liquid formulations for parenteral administration [5],

Developed for human pharmaceutical compounds, the Biopharmaceutics Classification System (BCS) is an important tool that facilitates product development and regulatory decisions. Within the framework of human pharmaceuticals, drugs can be classified into the following four BCS categories:**Class I:** high solubility, high permeability: generally, very well-absorbed compounds. **Class II:** low solubility, high permeability: exhibits dissolution rate-limited absorption. **Class III:** high solubility, low permeability: exhibits permeability-limited absorption. **Class IV:** low solubility, low permeability: very poor oral bioavailability[6], [7].

### Chemical And physical Properties of ASA

ASA is an odorless, colorless to white, crystalline powder with the chemical formula  $C_9H_8O_4$ [8]. It is a phenolic acid compound, is a metabolite of salicin, one of the oldest pain relievers derived from willow bark. At the same time, it is a precursor of a well-known drug, ASA is widely used as an intermediate for the production of many industrial compounds. In this sense, salicylic acid is one of the active ingredients in cosmetic products [9] soluble in ethanol, ether, acetone, chloroform, methanol, and slightly soluble in water with melting range: - 135-136 °C

ASA has a chiral center, although it is typically used as a racemic mixture, the compound primarily acts as a nonsteroidal anti-inflammatory drug through the inhibition of cyclooxygenase

(CO<sub>x</sub>) enzymes, which leads to a reduction in the synthesis of prostaglandins[10].

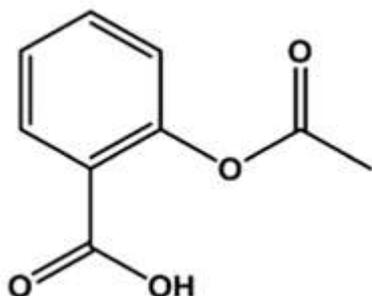


Figure 1. Aspirin structure

## II. MATERIAL AND METHOD

ASA was selected for the study of effect of salt on the physicochemical parameter of the selected drug. The salts such as NaCl, CaCl<sub>2</sub>, MgCl<sub>2</sub> and FeCl<sub>3</sub> were used in different concentration. Double distilled water is used for preparation of solution mixture. The distillation of water was carried out using a pinch of KMnO<sub>4</sub> & KOH in glass quick fit apparatus. The density and viscosity of water are measured at 298.15 K and 303.15 K and compared with literature values. Apparatus and procedure Densities of liquids and various solutions were measured at 301.5K by using specific gravity bottle of 10 cm<sup>3</sup> capacity. A single pan electronic balance [Sansui; model KD-UBED of capacity 120 gm and with a precision of 0.0001 gm] was used for weighing purpose. The

weighing was repeated thrice to ensure the accuracy in weights with a little interval of time. The reproducibility of the result was close to hundred percent. Viscosity measurements were carried out using Ostwald's viscometer with precision  $\pm 0.1$  %. The viscometer was clamped vertically in a thermostatically controlled water-bath, whose temperature was maintained constant at 301.5K ( $\pm 0.02^\circ\text{C}$ ). A fixed volume (10ml) of the solution was delivered into the viscometer. The viscometer was kept for 30 minutes in the thermostatically controlled water-bath to achieve constant temperature. The experimental measurements of flow time of the solution between two points on the viscometer were performed at least three times for each solution and the average results were noted

## III. THE RESULT OF STUDY

### 3.1 The results of physicochemical properties of ASA drug

The results of physicochemical properties of ASA drug in aqueous solution without any additives are shown in Table 2. This showed that solubility, densities, viscosity and conductance were increased with increasing in the concentration of ASA solution, several studies have shown the physicochemical properties of drug[11].

Temperature: -27 °C

Drug: - ASA solution

Table 2. Properties of ASA solutions in absence of additives

Sr. NO	Wight (g) of ASA in 100 ml	Solubility in molarity (mol/L)	Density g/ml	Viscosity (centipoise)	Observed Conductance (millimhos)
1	0.01	0.0012	0.964	1.035253	0.09
2	0.2	0.0060	0.965	1.11035	0.480
3	0.6	0.0249	0.966	1.139288	0.680
4	1	0.0276	0.9665	1.16768	0.683

### 3.2 Effect of sodium chloride on the physicochemical properties of ASA solution

The addition of sodium chloride (NaCl) (the concentration was increasing from 0.02 M to 0.08 M) to a ASA solution can have an impact on the physicochemical properties of the compounds, the effect of NaCl salt on the solubility and stability of ASA was investigated, the results showed that the solubility of ASA solutions was increased with increasing NaCl concentration, investigated the effect of NaCl on the solubility, density, viscosity and conductivity of drug solutions, the results showed that NaCl had a significant impact on these properties, with changes observed in the density, viscosity and conductivity of the solutions [12], the results showed increased with increasing NaCl, the results showed that the solubility was increasing from 0.0013 M to 0.0290 M (Table 3), the density was increasing from 0.965 g/ml to 0.970 g/ml (Table 4), the viscosity B-coefficient was increasing from 0.080857 to 0.153503 (Table 6) and the percent of degree of dissociation was increasing from 7.5 to 57.5 (table 8), there have been several studies investigating the effect of sodium chloride on the physicochemical properties of drug solution [13].

### 3.3 Effect of adding calcium chloride on the physicochemical properties of ASA solution

The addition of calcium chloride (CaCl<sub>2</sub>) (the concentration was increasing from 0.02 M to 0.08 M) to a ASA solution can impact the physicochemical properties, it was investigated, the results showed that the solubility, density and viscosity of ASA solutions were increased with increasing CaCl<sub>2</sub> concentration, the results showed that the solubility was increasing from 0.0015 M to 0.0290 M, the density was increasing from 0.966 g/ml to 0.971 g/ml (Table 4), the viscosity B-coefficient was increasing from 0.113962 to 0.173 (Table 6) and the percent of degree of dissociation was increasing from 17.8 to 73.57 (Table 8), studies have shown that the presence of calcium chloride can alter the interactions within the

solution, leading to changes in the physical characteristics of ASA formulations [14].

### 3.4 Effect of adding magnesium chloride on the physicochemical properties of ASA solution

The addition of magnesium chloride (MgCl<sub>2</sub>) (the concentration was increasing from 0.02 M to 0.08 M) to a ASA solution can impact the physicochemical properties, it was investigated and influence the solubility, density, viscosity and conductivity of ASA solutions, the results showed that the solubility, density and viscosity of ASA solutions were increased with increasing MgCl<sub>2</sub> concentration, the results showed that the solubility was increasing from 0.0023 M to 0.0300 M (Table 3), the density was increasing from 0.966 g/ml to 0.972 g/ml (Table 4), the viscosity B-coefficient was increasing from 0.14768 to 0.182137 (Table 6) and the percent of degree of dissociation was increasing from 21.9 to 97 (table 8), studies have shown that the presence of MgCl<sub>2</sub> can alter the interactions within the solution, leading to changes in the physical characteristics of ASA formulations [15].

### 3.5 Effect of adding iron (III) chloride on the physicochemical properties of ASA solution

The addition of calcium chloride (FeCl<sub>3</sub>) (the concentration was increasing from 0.02 M to 0.08 M) to a ASA solution can impact the physicochemical properties, it was investigated and influence the, viscosity and conductivity of ASA solutions, the results showed that the solubility, density and viscosity of ASA solutions were increased with increasing FeCl<sub>3</sub> concentration, the results showed that the solubility was increasing from 0.0554 M to 0.2800 M (Table 3), the density was increasing from 0.967 g/ml to 0.978 g/ml (Table 4), the viscosity B-coefficient was increasing from 0.18686 to 0.213806 (Table 6) and the percent of degree of dissociation was increasing from 33.4 to 98.7 (Table 8), studies have shown that the presence of FeCl<sub>3</sub> can alter the interactions within the solution, leading to changes in the physical characteristics of ASA formulations [16].

**Table-3. Solubility (mol /L) of ASA solutions in presence of additives**

Solubility of drug	NaCl (mol /L)			CaCl <sub>2</sub> (mol /L)			MgCl <sub>2</sub> (mol /L)			FeCl <sub>3</sub> (mol /L)		
	0.02	0.06	0.10	0.02	0.06	0.10	0.02	0.06	0.10	0.02	0.06	0.10
0.0012	0.0013	0.0015	0.0018	0.0015	0.0016	0.0018	0.0023	0.0043	0.0050	0.0554	0.127	0.2630
0.0060	0.0130	0.0150	0.0190	0.0140	0.0170	0.0135	0.0157	0.0175	0.0155	0.066	0.1726	0.2700
0.0249	0.0260	0.0280	0.0285	0.0265	0.0265	0.0285	0.0270	0.0280	0.0295	0.077	0.179	0.2780
0.0276	0.0280	0.0290	0.0290	0.0285	0.0285	0.0290	0.0290	0.0290	0.0300	0.077	0.1910	0.2800

**Table-4 Densities (g/ml) of ASA solutions in presence of additives**

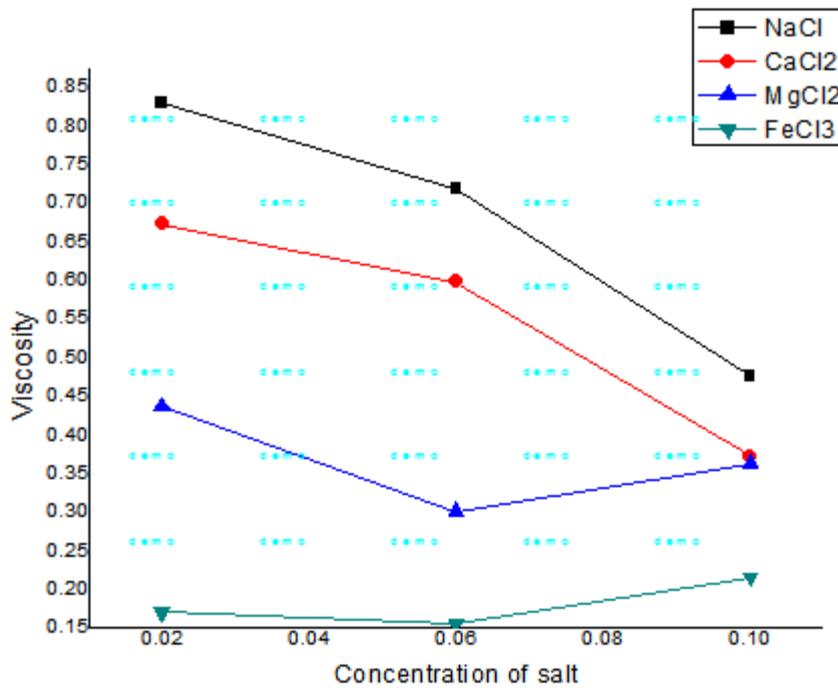
Density of drug	NaCl (mol /L)			CaCl <sub>2</sub> (mol /L)			MgCl <sub>2</sub> (mol /L)			FeCl <sub>3</sub> (mol /L)		
	0.02	0.06	0.10	0.02	0.06	0.10	0.02	0.06	0.10	0.02	0.06	0.10
0.964	0.965	0.967	0.967	0.966	0.967	0.968	0.966	0.968	0.968	0.967	0.968	0.971
0.965	0.966	0.967	0.967	0.968	0.969	0.970	0.968	0.969	0.971	0.968	0.971	0.972
0.966	0.967	0.968	0.969	0.969	0.969	0.9705	0.968	0.970	0.9715	0.969	0.972	0.973
0.9665	0.968	0.969	0.970	0.969	0.970	0.971	0.969	0.971	0.972	0.970	0.972	0.973

**Table-5. Viscosities (centipoise) of ASA solutions in presence of additives**

Viscosity of drug	NaCl (mol /L)			CaCl <sub>2</sub> (mol /L)			MgCl <sub>2</sub> (mol /L)			FeCl <sub>3</sub> (mol /L)		
	0.02	0.06	0.10	0.02	0.06	0.10	0.02	0.06	0.10	0.02	0.06	0.10
1.035253	1.07141	1.11065271	1.147674	1.105943	1.129341	1.169492211	1.14094	1.178509	1.187774349	1.188398	1.204451	1.217477897
1.11035	1.127996	1.14767447	1.184696	1.152785	1.1707	1.197950928	1.176656	1.203841	1.200749193	1.197039	1.217478	1.224313713
1.139288	1.166185	1.17665634	1.192711	1.189283	1.183708	1.20042956	1.195186	1.20694	1.218104816	1.203841	1.224314	1.229298442
1.16768	1.198892	1.22795463	1.231079	1.204149	1.233294	1.238289818	1.207551	1.232348	1.246641623	1.216224	1.228035	1.257237043

**Table 6. Viscosity B-Coefficient in presence and absence of additives**

	Concentration(M)	A	B
Without additives	-	0.842366	0.053222
NaCl	0.02	0.830041	0.080857
	0.06	0.717846	0.11223
	0.10	0.475153	0.153503
CaCl <sub>2</sub>	0.02	0.672345	0.113962
	0.06	0.597527	0.134866
	0.10	0.37246	0.173011
MgCl <sub>2</sub>	0.02	0.436703	0.147648
	0.06	0.300443	0.182137
	0.10	0.363571	0.184588
FeCl <sub>3</sub>	0.02	0.169794	0.186862
	0.06	0.156258	0.205399
	0.10	0.215874	0.213806



**Figure 2**

Figure 2-A coefficient, related to long-range ion-ion electrostatic interactions.

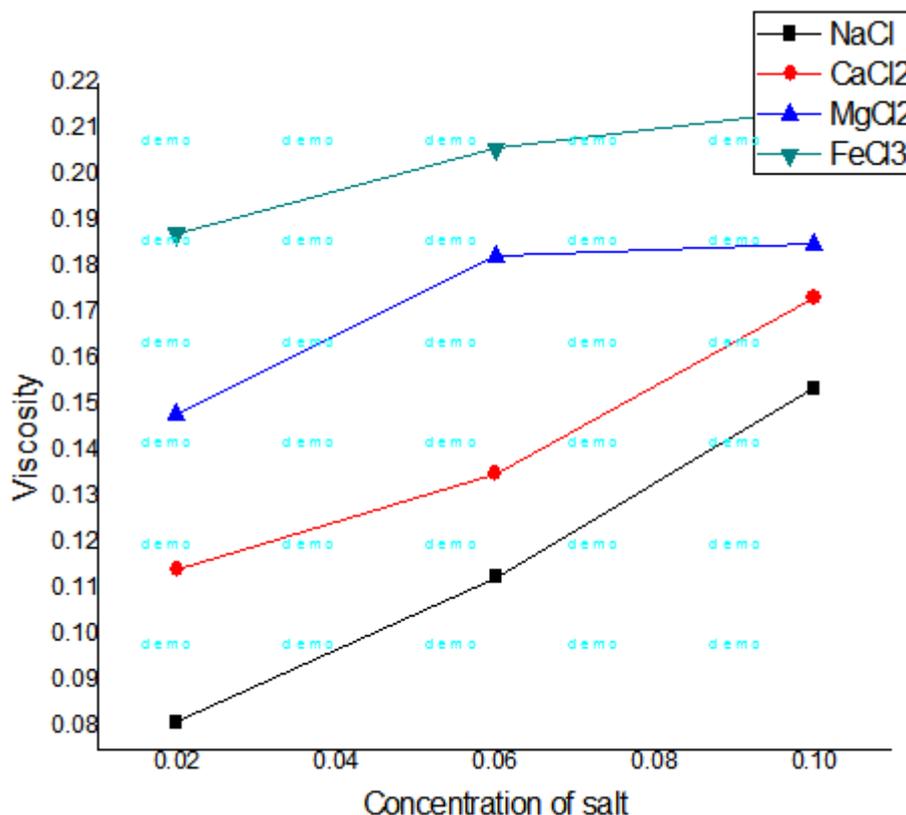


Figure 3

Figure 3-B coefficient, related to short-range ion-solvent

The A and B coefficient in the Table 6 (Viscosity B-Coefficient in presence and absence of additives) come from the Jones-Dole equation, which describes how the viscosity of an electrolyte solution changes with concentration:

$$\frac{\eta}{\eta_0} = 1 + A\sqrt{c} + Bc$$

where:

- $\eta$  = viscosity of the solution
- $\eta_0$  = viscosity of the pure solvent (water)
- $c$  = molar concentration of solute ( $\text{mol}\cdot\text{L}^{-1}$ )
- A = Falkenhagen coefficient (accounts for ion-ion interactions)
- B = Jones-Dole coefficient (accounts for ion-solvent interactions)

Table-7. The percent of dissociation of ASA in presence of additives

ASA	NaCl (mol /L)			CaCl <sub>2</sub> (mol /L)		
	0.02	0.06	0.10	0.02	0.06	0.10
1.388032	21.74584	57.52622	32.69587	31.30783	73.5657	70.01851
3.701419	13.95743	30.22825	30.92227	17.81308	41.40962	43.72301
3.495784	9.561999	20.9233	30.89657	28.84022	29.09727	42.56632
2.633405	7.518507	22.90253	27.41363	33.15854	34.62369	34.12246
ASA	MgCl <sub>2</sub> (mol /L)			FeCl <sub>3</sub> (mol /L)		
	0.02	0.06	0.02	0.06	0.02	0.06
1.388032	37.78532	77.42134	37.78532	77.42134	37.78532	77.42134
3.701419	21.90006	49.42936	21.90006	49.42936	21.90006	49.42936
3.495784	29.35431	33.77545	29.35431	33.77545	29.35431	33.77545
2.633405	33.58267	34.35379	33.58267	34.35379	33.58267	34.35379

#### IV. CONCLUSION

The study demonstrates the addition of inorganic salts such as NaCl, CaCl<sub>2</sub>, MgCl<sub>2</sub>, and FeCl<sub>3</sub> significantly alters the physicochemical properties of ASA solutions. Across all cases, increasing salt concentration led to enhanced solubility of ASA, increment in density, increased viscosity B-coefficient which indicating enhanced ion-solvent interactions and greater structuring effect of the salts on water and also improved degree of dissociation, suggesting stronger ionization of ASA in the presence of salts, which stabilizes the dissolved state.

Among the salts tested, the effect followed the trend: FeCl<sub>3</sub> > MgCl<sub>2</sub> > CaCl<sub>2</sub> > NaCl

This order reflects the increasing charge density and hydration ability of the cations, with Fe<sup>3+</sup> showing the most pronounced influence due to its strong ion-solvent interactions. Overall, the results highlight that electrolyte addition enhances the solubility, stability, and dissociation of ASA solutions, which is valuable for understanding drug behavior in biological fluids and for improving pharmaceutical formulations.

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