

STUDY OF INTERACTION OF DRUGS WITH BODY-ALIKE MACROMOLECULE (POLYVINYLPIRROLIDONE) BY ULTRA VIOLET SPECTROSCOPIC METHOD

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UV-visible spectrophotometric technique was used to study the interaction of polyvinylpyrrolidone (PVP) with co-solutes: phenol, benzoic acid, sodium benzoate, salicylic acid and acetyl salicylic acid in aqueous medium. Changes in the absorption spectra of the co-solutes were observed in the presence of PVP from 200 to 210 nm. The changes were attributed to interaction of PVP molecules with the co-solute molecules. As the concentration of the co-solute increased, a red shift in the bands was observed indicating an increase in interaction between PVP and the co-solute.

Keywords: Polyvinylpyrrolidone, Phenol, Benzoic acid, Acetyl salicylic acid, UV-visible spectrometry

INTRODUCTION

Polyvinylpyrrolidone (PVP) is a water soluble nonionic polymer. This polymer has both hydrophilic and hydrophobic characters and therefore, is known as amphiphilic polymer. PVP has large scale industrial applications and is used in pharmaceuticals, cosmetics and engineering products. PVP monomer is structurally related to protein and has been suggested as a synthetic polymer model for proteins (Jirgenson 1952).

The use of PVP in drugs is important as it may affect the delivery, release and efficacy of drugs. The presence of PVP has been shown to increase the solubility and dissolution rates of certain poorly soluble drugs such as prednisolone, nitrofurantoin and nitrofurazone (Bogdanora, Lambov and Minkov 1981). PVP is also used as a binder or granulator in tablets because of its cohesive properties. Highest shelf life has been reported for

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ascorbic acid tablets containing PVP as a binder (Shukla and Varma 1983). Generally it is believed that polar carbonyl groups of PVP are responsible for interaction with other polar compounds through hydrogen bonding. Molyneux and coworkers studied the interaction of PVP with ionic and nonionic compounds in aqueous medium (Molyneux and Frank 1961a, 1961b, 1964; Molyneux and Cornarakis-Lentzos 1979; Molyneux and Vekayanondha 1986a, 1986b). They concluded that hydrogen bonding is responsible for the interaction of PVP and co-solutes. Kahela and Forson (1971) carried out NMR and IR study of the interaction of PVP with benzoic acid and salicylic acid. They concluded that hydrogen and hydrophobic bonds are present in both PVP-benzoic acid and PVP-salicylic acid systems.

Interaction of PVP with copper, nickel and cadmium dodecyl sulfate surfactants was recently colorimetrically investigated (Bury and Treiner 1994). Ahmad (2004) has studied PVP interactions with *bis*-azo dye in aqueous solution.

The present study was carried out with an objective to specifically locate interaction sites in the PVP chain and co-solutes. Thus, the complexity of the co-solute was changed from phenol with one hydroxyl group to acetyl salicylic acid having carboxylic and acetyl groups.

MATERIALS AND METHODS

PVP sample with an average molecular weight of 44,000 was purchased from BDH (England). PVP was dried in the oven for one hour at 50°C before use because of its hygroscopic character. Phenol was obtained from Peking Chemical Work (China) while benzoic acid, sodium benzoate, acetyl salicylic acid and salicylic acid were obtained from Merck and BDH (England), respectively. All chemicals were of analytical grade and used without further purification and doubly distilled water was used as a solvent Shimadzu UV-160A, double beam UV-Vis spectrophotometer with measuring wavelength (λ) range of 200 to 1100 nm and wavelength accuracy of ± 0.5 nm was used for absorption measurements. Square quartz cells with 1 cm path length were used throughout the work. All measurements were carried out at room temperature ($25 \pm 2^\circ\text{C}$). Concentration of polymer solution was fixed at 5×10^{-3} g/dL while concentrations of the co-solutes were varied from 1.5×10^{-3} to 4×10^{-3} g/dL.

RESULTS AND DISCUSSION

Phenol solution in aqueous medium showed two bands in UV spectrum. These bands occurred near 210 nm and 270 nm (Fig. 1). Phenol spectra in presence of 88 PVP (5×10^{-3} g/dL) were also recorded. As concentration of phenol in PVP-phenol system was increased, a significant red shift was observed (Fig. 2).

For aqueous benzoic acid solution two bands, one near 227 nm and another near 275 nm were recorded (Fig. 3). In presence of PVP a shoulder at 202 nm appeared which red shifted on increase of benzoic acid concentration in the system. No significant shift in other bands was observed (Fig. 4). Sodium benzoate solutions were also run for λ_{\max} values. It showed λ_{\max} near 224 nm and 270 nm (Fig. 5). In the presence of PVP a shoulder near 200 nm appeared and red shifted with increase of sodium benzoate concentration in the system (Fig. 6).

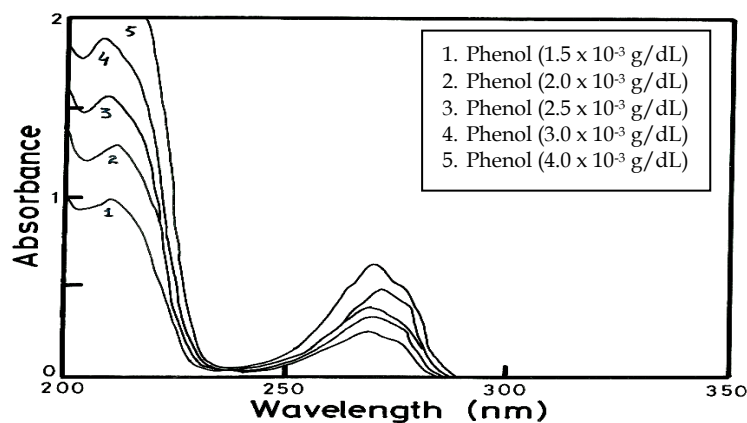


Fig. 1: UV absorption spectra of phenol in water, each recorded versus water as reference.

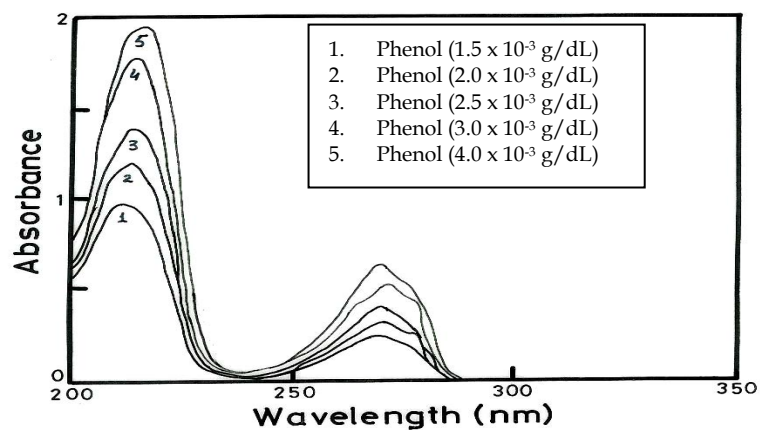


Fig. 2: UV absorption spectra of phenol in presence of PVP (5.0×10^{-3} g/dL), each recorded versus solution containing 5.0×10^{-3} g/dL PVP as reference.

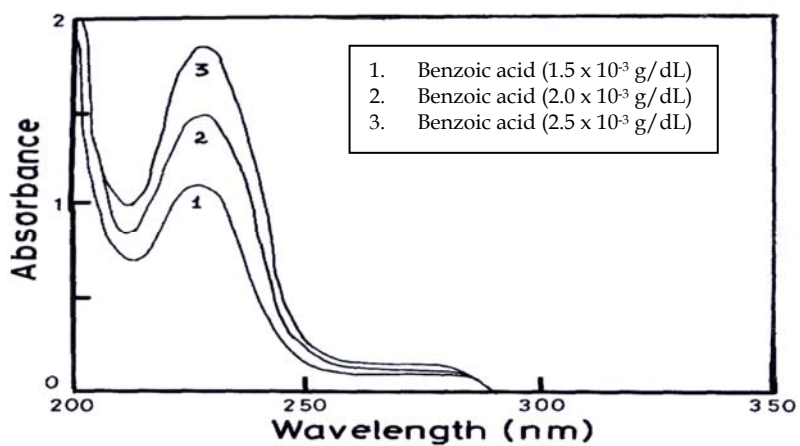


Fig. 3: UV absorption spectra of benzoic acid in water, each recorded versus water as reference.

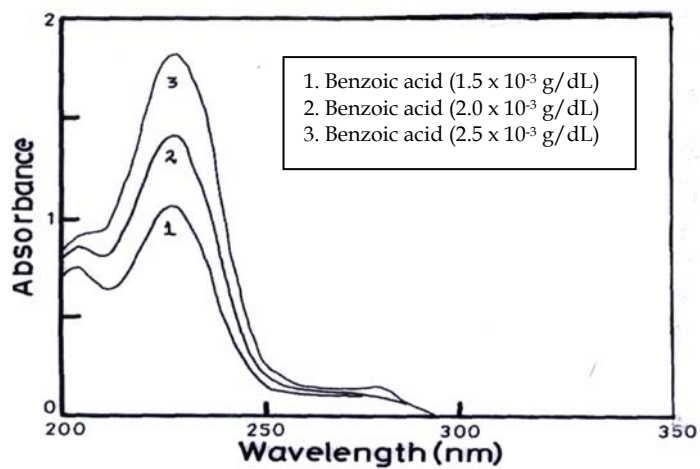


Fig. 4: Absorption spectra of benzoic acid in presence of PVP (5.0×10^{-3} g/dL), each recorded versus solution containing 5.0×10^{-3} g/dL PVP as reference.

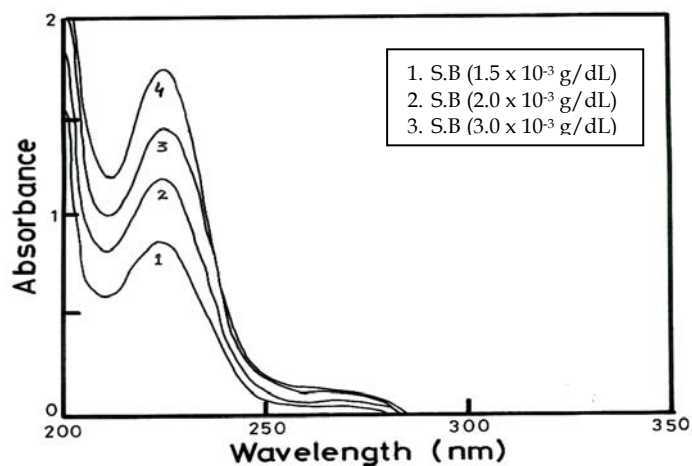


Fig. 5: UV absorption spectra of sodium benzoate (S.B) in water, each recorded versus water as a reference.

For salicylic acid two bands, one near 232 nm and another at 296 nm were recorded (Fig. 7). In the presence of PVP a band near 209 nm appeared in the absorption range of the instrument. This band red shifted with increase in concentration of salicylic acid in the PVP-salicylic acid system (Fig. 8). Spectra of acetyl salicylic acid are shown in (Fig. 9). Acetyl salicylic acid gave a λ_{\max} near 274 nm and a shoulder near 230 nm. In presence of PVP a peak near 207 nm was also observed. The peak near 207 nm was red shifted as concentration of acetyl salicylic acid was increased (Fig. 10).

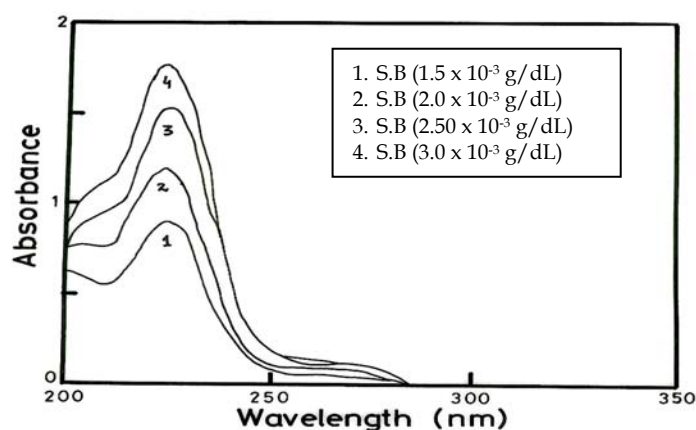


Fig. 6: UV absorption spectra of sodium benzoate (S.B) in presence of PVP (5.0×10^{-3} g/dL), each recorded versus solution containing 5.0×10^{-3} g/dL PVP as reference.

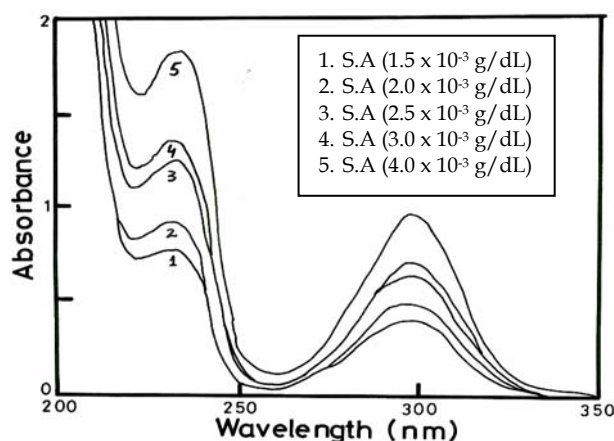


Fig. 7: UV absorption spectra of salicylic acid (S.A) in water, each recorded versus water as reference.

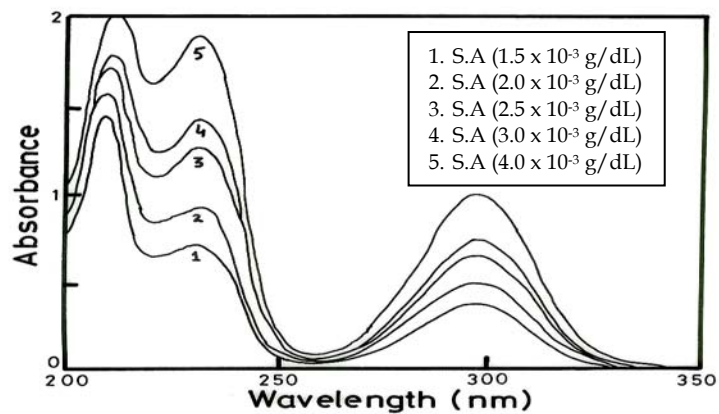


Fig. 8: UV absorption spectra of salicylic acid (S.A) in presence of PVP (5.0×10^{-3} g/dL), each recorded versus solution containing 5.0×10^{-3} g/dL PVP as reference.

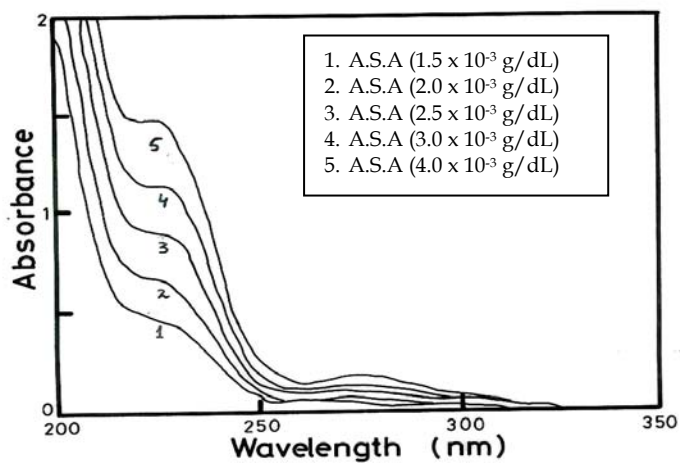


Fig. 9: UV absorption spectra of acetyl salicylic acid (A.S.A.) in water, each recorded versus water as reference.

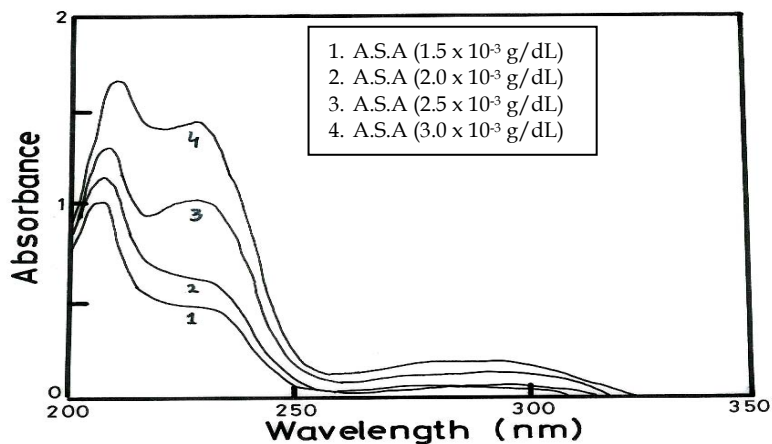


Fig. 10: UV absorption spectra of acetyl salicylic acid (A.S.A) in presence of PVP (5.0×10^{-3} g/dL), each recorded versus solution containing 5.0×10^{-3} dL PVP as reference.

All co-solutes are aromatic compounds and have common benzene chromophore. Functional groups attached to benzene ring are hydroxyl, carboxylic acid acetyl, which are auxochromes. Benzene has two types of bands i.e., primary at 184 nm (second primary) and 202 nm (first primary) and secondary band at 254 nm. All these bands are due to π - π^* transition (Silverstein, Bassler and Morrill 1974). Substitution of functional groups or auxochromes on benzene ring caused shifts in these bands.

In phenol, a 7 nm shift in first primary and a 16 nm shift occurred in secondary band, while in benzoic acid a 24 nm shift in first primary and a 20 nm shift in secondary band occurred.

These shifts are due to interactions of nonbonding electrons on hydroxyl group with π electrons of the benzene ring and conjugation of π electrons of carboxylic group with π electrons of benzene ring respectively (Silverstein, Bassler and Morrill 1974).

In sodium benzoate first primary band shifts by 21 nm and secondary band shifts by 16 nm. These shifts are comparatively smaller than benzoic acid. Sodium benzoate dissociates in aqueous solution and forms benzoate ions. These benzoate ions possess negative charge on its carboxylic group and so electrons are less available for transfer and make resonating structures. That is why sodium benzoate shows less red shift compared to benzoic acid both in first primary and secondary bands.



Fig. 11: resonating structures of carbonyl group.

For salicylic acid a 29 nm shift in first primary and 42 nm in secondary band occurred. Carboxylic and hydroxyl groups are at *ortho* position and there is greater probability of intramolecular hydrogen bonding, which, also affected its acidic character (Worly 1993). Greatest red shifts in both primary and secondary bands were observed for salicylic acid. In acetyl salicylic acid first primary band shifts by 27 nm and secondary band by 20 nm. Absorption intensity of secondary band is low and is not well defined since acetyl and carboxylic groups are both electron withdrawing and *ortho* to each other. Due to possibility of intramolecular hydrogen bonding between acetyl and carboxylic group, first primary band is red shifted to greater extent compared to phenol and benzoic acid (Worly 1993). PVP has lactam carbonyl group ($>N-C=O$) which is important from interaction point of view. This group has two resonating structures A and B (Turker, Guner and Guven 1990).

PVP has two interacting sites; in structure A, carbonyl group can form hydrogen bond while in structure B the positive charged nitrogen can electrostatically interact (Fig. 11).

Considering co-solute spectra, one can observe two important changes in the presence of PVP. The second primary band shifts to higher wavelengths and absorption intensity of these bands also decreases. As the co-solutes are both in ionized as well as in unionized form, the anions formed can interact electrostatically with the positive charged nitrogen of the pyrrolidone ring. Similarly the unionized forms of co-solutes have partially positive hydrogen atoms which can interact with the lactam carbonyl group and may form hydrogen bonds.

Hydrogen bonding affects $\pi-\pi^*$ transition and it makes red shift (Iwata and Morokuma 1973). In most $\pi-\pi^*$ transitions the excited state is more polar than the ground state (Pavia, Lampman and Kriz 1979). On

formation of hydrogen bonds with PVP the excited state of co-solute is more stabilized compared to the ground state and as a result the energy gap between the ground state and excited state decreases and as a result a red shift is observed on the introduction of PVP to the aqueous co-solute solution. On increase of co-solute concentration this red shift is further increased indicating increased stability in π^* state.

CONCLUSIONS

The results show that in presence of PVP the red shift in second primary band is due to the interaction of PVP with co-solutes. Further red shifts in these bands with increase in concentration of co-solutes are due to increase in interaction. It is hoped that further exploration of interactive properties of PVP with these co-solutes will provide deep insight and further studies are needed to confirm this.

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