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Molecular Interaction Activities of Phenylephrine Hydrochloride with Aqueous System by using Physicochemical Properties at 298.15, 303.15, 308.15 and 313.15 K

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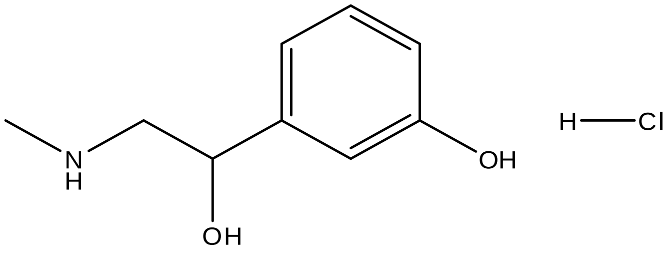
Abstract: The solubilizing tendency of the phenylephrine hydrochloride (PHC) with water was supported by the intermolecular interaction (IMI). The effect of PHC concentration with water molecules on the interaction by using physicochemical properties (PCP) was investigated at 298.15, 303.15, 308.15 and 313.15 K. The PCP such as density (ρ, g cm^{-3}), Apparent Molar Volume (V$_\phi$,cm^3·mol^{-1}), viscosity (η, mPa.s), and surface tension (γ,mNm^{-1}) of PHC in aqueous solution have been determined at 298.15, 303.15, 308.15 and 313.15 K. The PCP determine the state of intermolecular forces (IMF) between PHC and water (W). The concentration of PHC ranged from 0.02- 0.10 millimolar (mM) as a binary system in water. This study shows molecular interaction mechanism moderated through PCPs to assess state of IMF produced on PHC-Water interaction at 298.15, 303.15, 308.15 and 313.15 K which revealed that structural potential of PHC with water responsible for develop interaction.

The PCP data confirms structural behavior of PHC with water for intermolecular interaction and increases with increasing concentration of PHC. The temperature dependent solubility determined at 298.15, 303.15, 308.15 and 313.15 K which indicates that on increasing temperature the significant change found in PCP. This is due to structure breaking effects of PHC with water furnished disruption of hydrogen bond (HB) in water and electrostatic interactions (EI).

Keywords: Physiochemical properties; Intermolecular interactions; phenylephrine hydrochloride; Intermolecular Forces.

I. INTRODUCTION

Recently, the solubility and interacting potential of drug molecules in aqueous system required to established various applications in the field of biomedical sciences [1].The solubility of a drug molecule basically depends on the structure of drug and nature of solvent besides on temperature and pressure [2-6]. The state of solubility of a drug in a definite solvent have been determined through saturation point of drug concentration in a solution [7]. The aqueous solubility of drug molecules plays an important role for maximum administration, distribution, high potency, least sterility limitations, and flexibility in the efficiency of formulation in dosage forms for achieving required pharmacological response [8-11]. The drug solubility creates a major challenge for the design of oral dosage-based formulations inferred their poor bioavailability [12-15]. The oral bioavailability of drugs depends on several features such as structural activities, water solubility, drug-protein binding, drug efficacy, absorptivity, dissolution proportion, systematic metabolism and sustainable drug delivery [16-19].



Phenylephrine hydrochloride

Fig.1. Molecular structureof Phenylephrine hydrochloride

The PHC is an official drug pharmacopoeia and commonly used in biopharmaceutical formulations for treatmentof common nasal decongestant in cold and flu to control unwanted indications and to relieve sinus congestion because of a-adrenergic activity [20-22]. In the molecular structure of PHC having functional moieties like one aromatic ring, one -OH which attached to ring, CH(OH)-CH_2-NH-CH_3 side chain and HCl (Fig.1). These functional moieties are responsible to enhanced bioavailability and interacting activities of PHC.This study focused on the role of structural features of PHC to develop interaction with water optimized through intermolecular interaction by generating Intermolecular Forces (IMF) at different concentration and temperature of the PHC-Water solution (T=298.15, 303.15, 308.15, 310.15 and 313.15).

Apparently, the interaction of PHCdetermined by using PCPs such as Density, Apparent Molar Volume, Viscosity, and Surface tension in aqueous solution have been determined at 298.15, 303.15, 308.15 and 313.15 K.

II. MATERIALS AND METHODS

A. *Materials*

Phenylephrine Hydrochloride (Sigma Alrich), Acetone (Renkem), and distilled water were used as received.

B. *Methods*

1) *Physicochemical Properties Characterization*

The drug-water solutions with different concentrations of PHC varied from 0.02-0.10 milli molar (mM) distinctly dissolved in distilled water and stirred for 15 minutes to get homogeneous solution with help of magnetic stirrer.Further PCPs were measured at 298.15, 303.15, 308.15 and 313.15 K temperatures to identify the interacting potential of PHC with water molecules and their stability as increasing temperature.

The PCPs such as density, apparent molar volume, viscosity, and which denotes the IMI potential of PHC with water at 298.15, 303.15, 308.15 and 313.15 K. The Anton Paar Density Meter (DSA 5000 M) was used to measure Densities and 3 mL sample was occupied in DSA Quartz U tube for separately measurement. To determine viscosity and surface tension, viscous flow times (VFT) and pendent drop numbers (PDN) respectively were measured with Borosil Mansingh Survismeter (BMS). For each measurement, temperature was controlled through Auto temperature-controlled LAUDA ALPHA RA 8 thermostat.

III. RESULTS AND DISCUSSION

A. *Physicochemical Study*

The PCPs shows the state of IMI in drug-solvent solutions to identify molecular interaction which is depend on the structural reorientations of PHC with water and further molecular motion sand reorientations generates during interactions. Also, the illustrative IMF which are develops because of intermolecular hydrogen bond, hydrophilic and ionic interactions. The determined PCPs of water, and PHC-W solutions were shown in tables 1 and2.These PCPs specifies molecular combinations in side interacting functional moieties as functions of solute-solvent and solute-solute interactions.

1) *Density (ρ)*

The ρ represents attraction forces due to development of IMF and shows internal pressure of the drug in the solvent. Theρ is regressed with mM/L by with Eq. (1).

$$\rho = \rho^{0} + S\rho\ m + S\rho^{'}\ m^{2} \qquad (1)$$

ρ° is limiting ρ at m → 0 and Sρ, Sρ'are the 1stand 2nddegree slopes.On increasing from 0.02-0.10 mM concentration of PHC in water, the ρ increases inferred that the development of internal pressure in PHC-W solution (Table.1).The 0.9969, 0.9953, 0.9938, 0.9921 g cm^{-3} ρ° values observed at temperatures 298.15, 303.15, 308.15 and 313.15 K respectively(Table.2) with 298.15 > 303.15 > 308.15 > 313.15 K trend. This revealed that the temperature dependent weakened internal pressure via IMI of PHC and solubility decreases in water because of higher disruption of HB interaction between PHC and W molecules at 313.15 K.The PHC having one six membered one aromatic ring, one -OH which attached to ring, CH(OH)-CH_2-NH-CH_3 side chain and HCl which develops stronger internal pressure in aqueous solution by interaction with water molecules produced highest ρ° value at 298.15. The weaker IMI via less structure breaking effects develop lower internal pressure in PHC-W solution resulted in the lowest ρ° at 313.15 K. However, at 298.15 K the higher ρ° value of PHC-W found as compared to at 313.15 K confirms theactivities of functional moieties present in the PHC which can recognized the stronger interacting activities with W. This ρ° variations due to state of internal pressure in PHC-W interactions, and thermal behavior also changes internal pressure and structure breaking effects on interaction of PHCwith water.

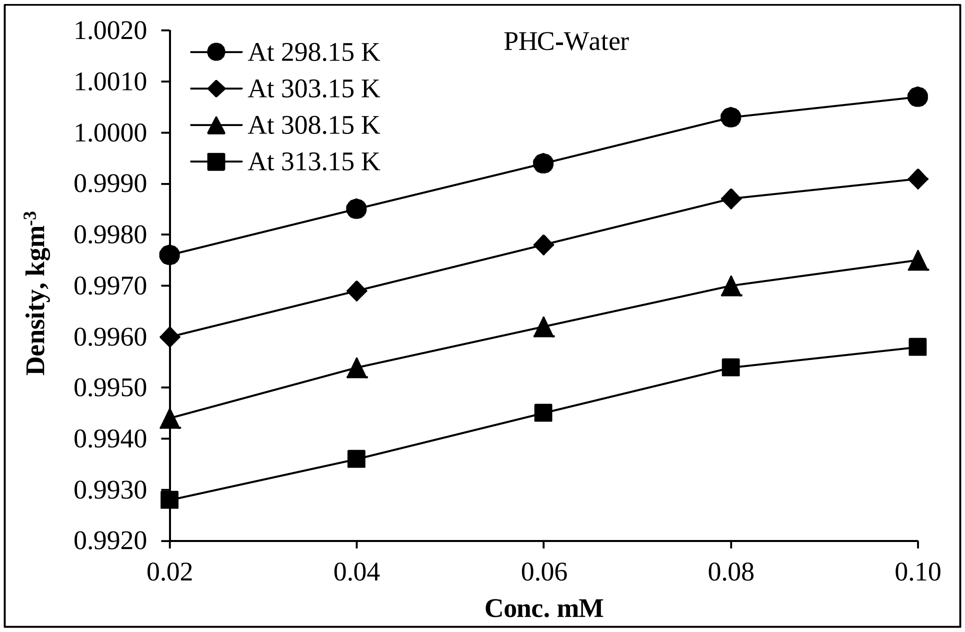


Fig.2. Densities of PHC + Water at 298.15, 303.15, 308.15 and 313.15 K.

The stability of IMI found at 298.15 K as compared to 303.15, 308.15 and 313.15 K. This inferred the role thermal behavior on interacting stability trough structure making and breaking activities of PHC with water due to additional functional moieties. Hence, the active functional moieties developed HB in PHC-W which furnished the disrupted water structure and forms higher IMI with higher internal pressure.The higher Sρ values in PHC-Water shows a stronger activity of structural framework on IMF that confirms the stronger structure breaking effects.

Table 1: Milli molar/L (mM), density ($\rho \pm 10^{-4}$ g cm^{-3}), Apparent Molar Volume (V_ϕ, $\pm 10^{-2}$cm$^{3}\cdot$mol^{-1}), viscosity ($\eta \pm 10^{-4}$mPa.s) and surface tension ($\gamma \pm 10^{-2}$mN m^{-1}) of PHC-W at 298.15, 303.15, 308.15 and 313.15 K.

mM	ρ	V_ϕ	η	γ
298.15 K				
0.02	0.9976	169.18	1.0345	70.95
0.04	0.9985	166.67	1.0799	70.49
0.06	0.9994	165.83	1.0930	70.04
0.08	1.0003	165.42	1.1127	69.59
0.10	1.0007	165.17	1.1450	69.11
303.15K				
0.02	0.9960	169.42	0.9138	69.19
0.04	0.9969	166.90	0.9555	68.76
0.06	0.9978	166.07	0.9676	68.34
0.08	0.9987	165.65	0.9857	67.92
0.10	0.9991	165.40	1.0154	67.48
308.15 K				
0.02	0.9944	169.69	0.8175	68.48
0.04	0.9954	167.17	0.8560	68.08
0.06	0.9962	166.33	0.8670	67.66
0.08	0.997	165.92	0.8836	67.26
0.10	0.9975	165.66	0.9110	66.84
313.15 K				
0.02	0.9928	170.00	0.7100	67.99
0.04	0.9936	167.48	0.7419	67.58
0.06	0.9945	166.64	0.7681	67.18
0.08	0.9954	166.22	0.8073	66.78
0.10	0.9958	165.96	0.8170	66.36

Table 2: Limiting density (ρ°, g cm^{-3}), 1st slope (S_ρ, kg^{2}m^{-3}mol^{-1}), Limiting Apparent Molar Volume (V_ϕ^o , m^3·mol^{-1}), 1st slopes ($S_{V\phi}$, kg$^{1/2}$·m^3·mol$^{-3/2}$). Limiting viscosity (η°, mPa·s), 1st slope (S_η, mPa·s kg m^{-1}) and Limiting surface tension (γ°, mN m^{-1}), 1st slope (S_γ, mN kg mol^{-1}m^{-1})

Temperature	ρ		V_ϕ		η		γ	
K	ρ°	S_ρ	V_ϕ °	S V_ϕ	η°	S_η	γ°	S_γ
298.15	0.9969	0.040	169.24	-46.39	1.0168	1.2694	71.41	-22.94
303.15	0.9953	0.040	169.47	-46.45	0.8976	1.1669	69.61	-21.32
308.15	0.9938	0.039	169.75	-46.52	0.8026	1.0733	68.89	-20.52
313.15	0.9921	0.039	170.05	-46.61	0.6851	1.3967	68.40	-20.37

2) *Apparent Molar Volume (V_ϕ)*

The apparent molar volume is important properties to identify the structural IMI developed in PHC-Water solution and differences in IMF which stimulated through the structural potential with increase in concentration of PHC in W. The V_ϕ(m^3/mol) was measured with densities and calculated with following Eq.(2).

$$V_\varphi = \frac{(\rho_0-\rho)}{m\rho_0\rho} + \frac{M}{\rho}(2)$$

The ρ_0 and ρ are the densities of solvent and solution respectively, m is the molarity of and M is the molar mass of PHC.The V_ϕ values are shown in table 2. The limiting apparent molar volume V_ϕ^0were found by using following Eq. (3).

$$V_\phi = V_\phi^{\ 0} + S_V m^{1/2} + S_V{}'m \quad (3)$$

TheV_ϕ^0 demonstrates the state of solute-solvent interaction, $S_V$and S_V' are slope value shows quantitative estimations of solute-solute interactions.

When concentration PHCwith water increases, the V_ϕ decreases due to weakening in solute-solvent interactions. At 298.15, 303.15, 308.15 and 313.15 K, $V\phi0$values 169.24, 169.47, 169.75, 170.05 m^3.mol^{-1}observed respectively.

TheV_ϕ^0 at 313.15 shows higher as compared to at 298.15 K for PHC-Water solution depicts resulted higher entanglement of water molecules within the structure of PHC during IMI.Also, weaker interactions between PHC-W causedbecause of solute-solute solvent interactionsin comparison with solvent-solvent interactions. This is due to functional moieties of PHC which encouragedPHC-W molecular reorientation through HB disruption mechanism of solute-solvent interactions also supported by their slope values (Table.2).

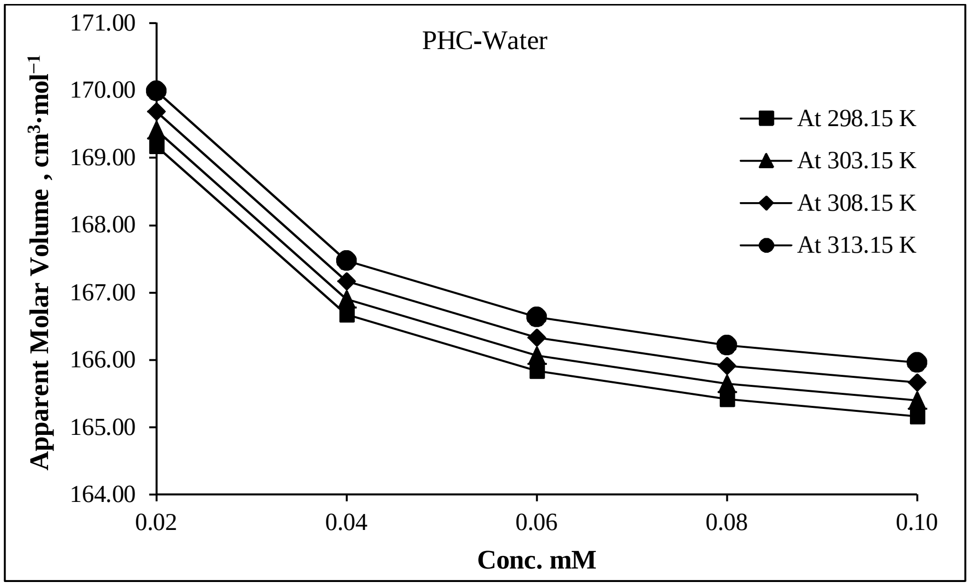


Fig. 3. Apparent Molar Volumeof PHC + Water at 298.15, 303.15, 308.15 and 313.15 K.

3) Viscosity (η)

The viscosity determines the state generated frictional force due to attraction between PHC-W which developed IMF in solution and resulted in higher η values with increasing concentration of PHC. For 0.02 mM to 0.10 mM concentrations of PHCwith water, the η was determined and calculated by using following Eq. (4).

$$\eta = \left(\frac{t}{t_0}\right)\left(\frac{\rho}{\rho_0}\right)\eta_0 \quad (4)$$

Where, η_0 is viscosity of a water, the t_0 and t are flow times of water and PHC-Watersolutions respectively. The η data were regressed with mM/L by using following Eq. (5) for determination of limiting viscosity and slopes.

$$\eta = \eta^0 + S\eta\, m + S\eta'\, m^2 \quad (5)$$

η^0 at m → 0 is limiting viscosity; S_η, S_η' are the 1stand 2nddegree of slope which determines state of IMF.The η, η^0 and $S_\eta$are tabulated in tables 1 and 2 and found that when concentration of PHCincreases in Water, then η values also increases which inferred the impact of structural functionalities in PHC to develop interaction caused in higher interacting activities with water at given temperature.

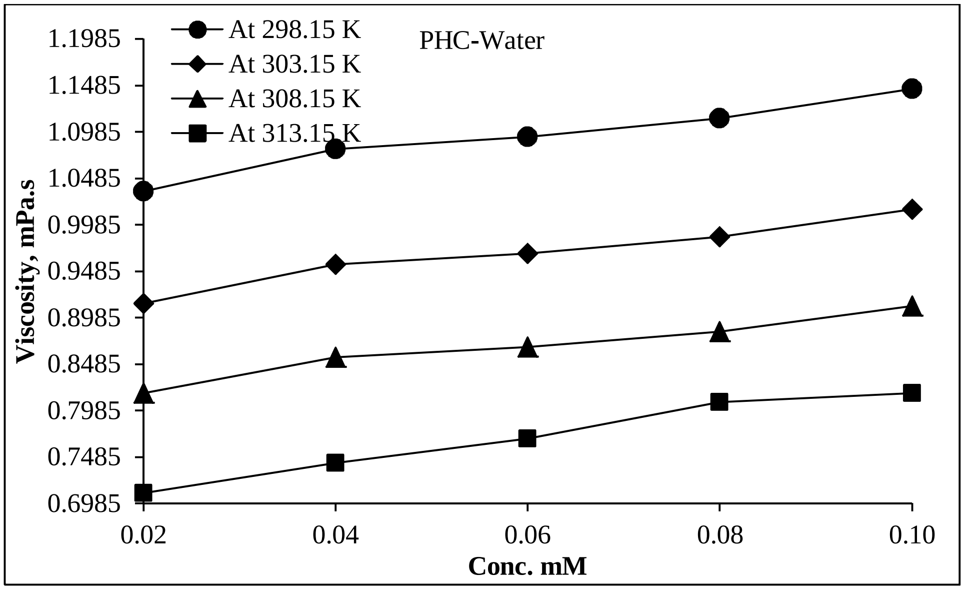


Fig. 4. Viscositiesof PHC + Water at 298.15, 303.15, 308.15 and 313.15 K.

The η°increases with decrease in temperature and the values found as 1.1342, 0.9657, 0.8157 and 0.6823 mPa.s at 298.15, 303.15, 308.15 and 313.15 K respectively (Table.2). The higher η° values is observed at 298.15 K as compared to 303.15, 308.15 and 313.15 K which confirms that therole of temperature to trigger functional moieties for development of FF. The higher FF in the PHC-Water solution shows the strong IMF are functioning for monitoring viscous fluid flow with increase in adhesive forces through capillary action. The higher FF and stronger IMF are due to PHC functionality strongly involved in IMT with water at different temperature and also accountable for the increased hydrogen bond and ionic interaction amongst PHC and Water. The aromatic ring with delocalized π electronic configuration, one -OH which attached to ring, $CH(OH)\text{-}CH_2\text{-}NH\text{-}CH_3$ side chain and HCl are responsible for the higher FF and caused stronger IMF. The decrease in η° with increase in temperature shifting of chargesand activates functional moieties in PHC. This can be concluded that the thermal energies are responsible to weakened interacting mechanism with disruption of HBI and changes in state of IMF. The limiting slopes, S_η values confirms the IMI of PHC and reinforced the state of IMF(Table.2).

4) Surface Tension (γ)

The attractive forces generated within solution and developed cohesive forces CF which resulted in lower surface tension values. This because of electrostatic forces and Vander walls forces obtained by engagements of PHC molecules within water. The γ for PHC-water were measured for 0.02 mM to 0.10 mM concentrations of PHC by measuring their PDN and determined with Eq. (6).

$$\gamma = \left(\frac{n_0}{n}\right)\left(\frac{\rho}{\rho_0}\right)\gamma_0 \quad (6)$$

The $\gamma_0$is surface tension of water, n_0 and n are PDN of water and PHC-water solutions respectively. The γ data are regressed to obtain limiting values $\gamma°$ at m→0 with the following Eq. (7).

$$\gamma = \gamma^0 + S\gamma\ m + S\gamma'\ m^2 \quad (7)$$

The limiting surface tension $\gamma°$, and $S\gamma$, $S\gamma'$are the 1st and 2nd degree slopes.The determined γ values of prepared 0.02 to 0.10 mM PHC-water solutions are given intable 1. The γ decreases with increasing concentration of PHC in water (Table 1 and Figure. 4). The lower $\gamma°$at 313.15 K illustratesstate of CF due to delocalized π-electrons generates electronic and coulombic interactions. The CF and FF signified higher interactions of PHC which is improved through IMF .This is due to structural activities of PHC-water and destabilized hydrophilic moieties and weakened favorable interactions caused in lower CFs .The structural potential of PHC molecules playing significant role to develop IMI and γ investigation confirmed by their surface activities through CF with strong attraction responsible to increased interacting activities.

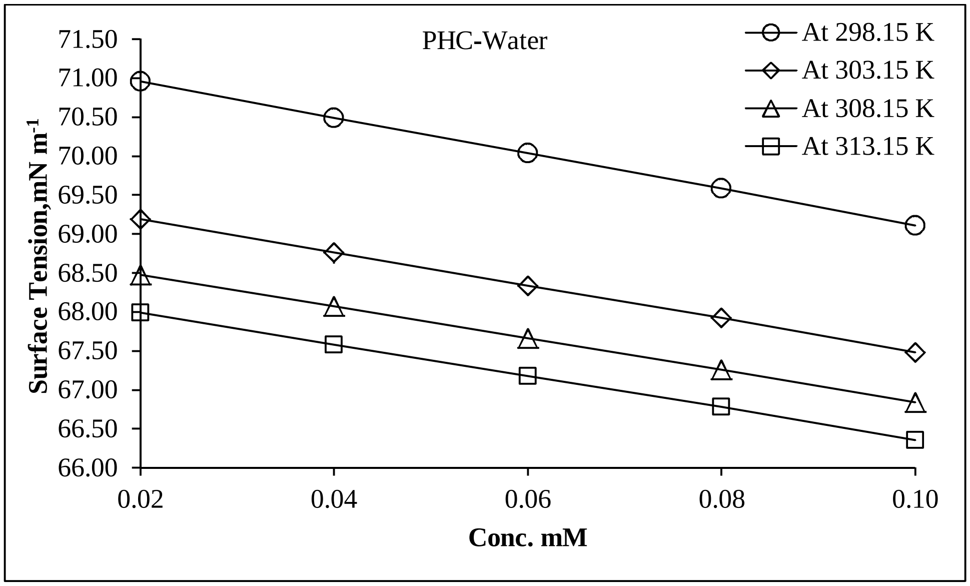


Fig. 5. Surface tensionof PHC + Water at 298.15, 303.15, 308.15 and 313.15 K.

IV. CONCLUSION

The physicochemical properties of PHC-Water were studied at 298.15, 303.15, 308.15 and 313.15 K. The remarkable variations in PCPs such as densities, apparent molar volume, viscosities and surface tensionwere in context the response of molecular structures of PHC increases the interaction activities with water. The growth of interaction exhibited the effects of dynamic functionality on increasing concentration of PHC in comparison with water medium confirmed HB operative and state of IMF for interaction activities.

The IMI of PHCwith water at 313.15 K PCPs are higher as compared to 303.15, 308.15 and 313.15 K have showed the important role of temperature and structural properties could be caused the FF and CF with strong IMF responsible for the IMI for stability of PHC with water over different temperature. The thermal activities has accountable for state of molecular reorientations in PHC-water which resulted in higher PCPs of PHC in water. The structural activities of PHC with water to improved and developed interactive Drug-Water formulations significant to enhance bioavailability of PHC for metabolic actions.

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