THERMODYNAMICS OF BINARY ALLOYS OF PHARMACEUTICAL ACTIVE IMIDAZOLE WITH O- PHENYLENEDIAMINE

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Abstract

The present study describes the investigation of eutectic and non-eutectic alloys of imidazole (IM) with o - Phenylendiamine (OPD). The solid-liquid equilibrium (SLE) data determined by thaw melt method in the form of melting temperature with their corresponding composition construct the solid-liquid equilibrium phase diagram which suggests simple eutectic behaviour is followed by the binary system. The activity co-efficient model based on enthalpy of fusion was employed to calculate the excess partial and integral thermodynamic functions such as $g^E$, $h^E$ and $s^E$. These values help to predict the nature of molecular interaction, ordering and stability between the components. The spontaneity of mixing of eutectic and non eutectic alloys was discussed by the partial and integral mixing quantities $\Delta G^M$, $\Delta H^M$ and $\Delta S^M$. Using Gibbs-Duhem equation the solution of partial molar heat of mixing, activity and activity coefficient of the component in the binary mix have been resolved.

Keywords: Phase diagram, Partial and integral thermodynamic functions, activity, activity co-efficient.

Introduction

Imidazole and its derivatives offer better pharmacodynamic characteristics1,2,3. It has been found that various recent new drugs developments in imidazole derivatives show better effect and less toxicity. The imidazole nucleus is an important synthetic strategy in drug discovery. Many imidazoles have been prepared as pharmacological agents, azomycine, clotrimazole, miconazol, ergothionine, clonidine and moxonidine. One of the most important applications of imidazole derivatives is to use as material for treatment of denture stomatitis. A number of compounds have been imidazole ring and exhibit different types of pharmacological and biological activities, like metronidazole and nitroimidazole as bactrical, 1-vinyl imidazole as fungical, megazol as trypanocidal, imidazol 2-one as antihelminical and other antimicrobial activities. It is incorporated into many important biological molecules. The most pervasive is the amino acid histidine, which has an imidazole side chain. Histidine is present in many proteins and enzymes and plays a vital part in the structure and binding functions of haemoglobin. The decarboxylated form of histidine is the histamine, which is also a common biological compound. It is a component of the toxin that causes urticaria which is another name for allergic hives. Theophylline molecule having imidazole nucleus is found in tea leaves and coffee beans that stimulates the central nervous system. It is also present in the anticancer medication mercaptopurine, which combats leukemia by interfering with DNA activities.

The high therapeutic properties of the imidazole drugs have encouraged the medicinal chemists to synthesise a large number of novel chemotherapeutic agents. Medicinal properties of imidazole aslo includes -lactamase inhibitors, 20-HETE (20 - Hydroxy - 5, 8, 11, 14 - eicosatetraenoic acid) synthase inhibitors, carboxypeptidase inhibitors, hemeoxygenase inhibitors antiaging agents, anticoagulants, anti-inflammatory, antiviral, antitubercular, antiidiabetic and antimalarial. The possible improvement in the biological activity of the compound can be further achieved by slide modification in the substituents of the basic imidazole nucleus. Keeping this view in mind, the imidazole(IM) based binary system with o – phenylendiamine(OPD) has been taken for detailed physico-chemical properties such as phase diagram, heat of fusion, activity, activity coefficient, excess and mixing thermodynamic functions.

Experimental Procedure

Imidazole (Merck, Mumbai) and o - Phenylendiamine (Qualigen) were taken as experimental materials and their purity were checked by comparing their melting points with the values reported in literature. Phase diagram of IM-OPD system was determined by the thaw melt method4,5. Mixtures of various composition of IM and OPD were prepared in long necked test tubes with closing the open ends and the mixture were homogenized by melting in silicon oil followed by chilling in ice. The test tubes were broken and the thaw and melting temperature of all mixtures were determined by using a Toshinval melting point apparatus and alloys were denoted by (A1, A2 ....... E.... Ag, A10 ). The heat of fusion of parent materials were determined by their DTA patterns6,7 obtained from Stanton Red Croft STA 780 series unit.

Results and Discussion

Phase Diagram

The solid-liquid equilibrium data for IM-OPD system are plotted in the form of temperature-composition curve as shown in Fig.1. The phase diagram exhibits the formation of simple eutectic. On addition of OPD into IM, the melting point of IM (88°C) decreases and attains a minimum (66°C) which is the eutectic temperature of the system. The eutectic composition is 0.34 mole fraction with respect to OPD. At the eutectic temperature both components separate out from the liquid phase (L) and a constant composition until the entire liquid phase disappear. Solution L is either saturated or is in equilibrium with both the solid phases (S1 and S2) and the system is invariant i.e. L $\rightarrow$ S1 + S2. At the eutectic temperature, the temperature of the solid is the same as that of liquid from which it separates out.
**Thermochemistry**

The behaviour of binary system and nature of interaction between the components forming alloy are very significant to solve the scientific and industrial problems involve the mixture behavior. It can be understood through data of heat of fusion, entropy of fusion, roughness parameter, mixing and excess thermodynamic values.

**Enthalpy of Fusion & Entropy of Fusion**

The enthalpy of fusion for each binary alloy is calculated by applying mixture law as given below:

\[ \Delta H_{\text{alloy}} = X_{\text{OPD}} \Delta H_{\text{OPD}} + X_{\text{IM}} \Delta H_{\text{IM}} \]

(1)

where \( X_{\text{OPD}} \) and \( X_{\text{IM}} \) are mole fractions and heat of fusion of OPD and IM are molal fractions and heat of fusion of \( \alpha \)-Phenylenediamine and Imidazole respectively.

The value of entropy of fusion \( (\Delta S) \) of each alloy has been calculated by the following relation:

\[ \Delta S = \frac{\Delta H}{T} \]

(2)

where temperature of the alloys. These values are reported in Table 1. The \( S \) values are positive in the cases under investigation an indicate an increase of randomness during melting.

**Activity & Activity Coefficient**

The activity coefficient of components OPD and IM for the alloys under investigation has been calculated from the equation given below:

\[ -\ln X_i^\gamma_i = \frac{\Delta H}{RT} \left( \frac{1}{T_i} - \frac{1}{T_c} \right) \]

(3)

where \( X_i^\gamma_i \) and \( T_i \) are the mole fraction and activity coefficient of the component \( i \) in the liquid phase respectively, \( T_c \) is the melting temperature of component \( i \) whereas \( T_e \) is the melting temperature of the alloy. The value of activity and activity coefficient of the components in the alloys are reported in Table 2.

**Mixing function**

Thermodynamic mixing functions of the binary alloys of the system were determined by using the following equation:

\[ \Delta G^M_i = RT \left( X_{\text{OPD}} \ln a_{\text{OPD}} + X_{\text{IM}} \ln a_{\text{IM}} \right) \]

(4)

\[ \Delta S^M_i = -R \left( X_{\text{OPD}} \ln X_{\text{OPD}} + X_{\text{IM}} \ln X_{\text{IM}} \right) \]

(5)

\[ \Delta H^M_i = RT \left( X_{\text{OPD}} \ln \gamma_{\text{OPD}} + X_{\text{IM}} \ln \gamma_{\text{IM}} \right) \]

(6)

\[ \Delta G^M_i = RT \ln a_i \]

where \( \Delta G^M \), \( \Delta S^M \) and \( \Delta H^M \) are integral molar free energy of mixing, molar entropy of mixing and molar enthalpy of mixing. \( G^M_i \) is the partial molar free energy of mixing of component \( i \) in binary mix. These values are reported in Table 3.

The negative values of molar free energy of mixing of all eutectic and non-eutectic alloys suggest that mixing in all cases is spontaneous. The integral molar enthalpy of mixing value corresponds to the values of excess integral molar free energy of the system favours the regularity in the binary solution.

**Excess thermodynamic functions**

The nonideal character of the binary mixture was detected by deviation of their activity coefficient from unity. The deviations from ideal behaviour can best be expressed in terms of excess thermodynamic functions, which give more quantitative idea about the nature of molecular interactions. This quantity represents the difference between the thermodynamic function of mixing for a real system and the corresponding values for an ideal system at the same temperature and pressure. It is denoted by subscript \( E \) and represents the excess of a given thermodynamic property of the solution over that in the ideal solution.

\[ y^E = \Delta y_{\text{mix}} \text{ (real) } - \Delta y_{\text{mix}} \text{ (ideal)} \]

(7)

where \( y \) can be taken as any of the thermodynamic functions. In order to know the nature of interaction between the components forming binary alloy, some thermodynamic functions such as integral excess free energy \( (g_E) \), excess enthalpy of mixing \( (h_E) \) and excess entropy of mixing \( (s_E) \) were calculated using the following equations:

\[ g^E = RT \left( x_{\text{OPD}} \ln \gamma_{\text{OPD}} + x_{\text{IM}} \ln \gamma_{\text{IM}} \right) \]

(8)

\[ h^E = -RT \left( x_{\text{OPD}} \ln \gamma_{\text{OPD}} + x_{\text{IM}} \ln \gamma_{\text{IM}} \right) \]

(9)

\[ s^E = R \left( x_{\text{OPD}} \ln \gamma_{\text{OPD}} + x_{\text{IM}} \ln \gamma_{\text{IM}} \right) \]

(10)

The value of \( \delta \ln \gamma_{\text{OPD}} / \delta T \) can be determined by the differentiation of equation (3).

\[ \delta \ln \gamma_{\text{OPD}} = \frac{\Delta H_{\text{OPD}}}{RT} - \frac{1}{X_i} \frac{\delta X_i}{\delta T} \]

(11)

Gibbs Duhem Equation

Gibbs Duhem Equation may be utilized to determine the activity, activity coefficient and partial molar enthalpy of mixing.

\[ \sum X_i \delta z_i = 0 \]

(12)

\[ X_{\text{OPD}} \frac{dH_{\text{OPD}}}{dM_{\text{OPD}}} + X_{\text{IM}} \frac{dH_{\text{IM}}}{dM_{\text{IM}}} = 0 \]

(13)

\[ \frac{dH_{\text{OPD}}}{dM_{\text{OPD}}} = \frac{X_{\text{OPD}}}{X_{\text{OPD}} + X_{\text{IM}}} \frac{dH_{\text{IM}}}{dM_{\text{IM}}} \]

The values of activity and activity coefficient of specific components in binary alloys can be determined by plotting graph between \( X_{\text{OPD}}/X_{\text{IM}} \) vs \( \ln a_{\text{OPD}} \) and \( X_{\text{OPD}}/X_{\text{IM}} \) vs \( \ln a_{\text{IM}} \) (Fig. 2, 3) where as a graph between \( X_{\text{OPD}}/X_{\text{IM}} \) and \( \Delta H_{\text{OPD}} \).
The phase diagram of IM-OPD system exhibits the formation of simple eutectic alloy. The molecular interaction between components in eutectic and non-eutectic alloys has been described in the light of \( g^8 \) value which suggests there are stronger association between like molecules in the binary mix. The negative value of \( \Delta G^M \) favours the spontaneous mixing in all the eutectic and non-eutectic alloys.

ACKNOWLEDGEMENTS

Thanks are due to the Head, Chemistry Dept., V. K. S. University, Ara 802 301 for providing research facilities.

REFERENCES


Table - 1 : Temperature-composition data, heat of fusion (\( \Delta H \)), entropy of fusion (\( \Delta S \)) of alloys of OPD-IM system.

<table>
<thead>
<tr>
<th>Alloy</th>
<th>Mole fraction of OPD</th>
<th>MP (K)</th>
<th>( \Delta H )</th>
<th>( \Delta S )</th>
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<td>356</td>
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<td>( \lambda_2 )</td>
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<td>353</td>
<td>14.25</td>
<td>40.39</td>
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<td>( \lambda_3 )</td>
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<td>347</td>
<td>14.97</td>
<td>43.16</td>
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<td>( \lambda_4 )</td>
<td>0.30</td>
<td>343</td>
<td>15.90</td>
<td>46.36</td>
</tr>
<tr>
<td>( \lambda_5 )</td>
<td>0.34</td>
<td>339</td>
<td>16.31</td>
<td>48.12</td>
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<td>( \lambda_6 )</td>
<td>0.39</td>
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<td>49.35</td>
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<tr>
<td>( \lambda_7 )</td>
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<td>344</td>
<td>17.24</td>
<td>50.11</td>
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<td>( \lambda_8 )</td>
<td>0.48</td>
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<td>17.75</td>
<td>51.01</td>
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<td>( \lambda_9 )</td>
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<td>353</td>
<td>18.88</td>
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<td>( \lambda_{10} )</td>
<td>0.72</td>
<td>365</td>
<td>20.22</td>
<td>55.40</td>
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Table - 2 : Values of Activity and Activity-coefficient of components in binary alloy of OPD-IM system.

<table>
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<tr>
<th>Alloy</th>
<th>( \ln a_{OPD} )</th>
<th>( \ln a_{IM} )</th>
<th>( \gamma_{OPD} )</th>
<th>( \gamma_{IM} )</th>
<th>( \ln a_{OPD} )</th>
<th>( \ln a_{IM} )</th>
<th>( a_{OPD} )</th>
<th>( a_{IM} )</th>
<th>( X_{OPD} )</th>
<th>( X_{IM} )</th>
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<td>( \lambda_1 )</td>
<td>2.418</td>
<td>-0.020</td>
<td>11.223</td>
<td>0.980</td>
<td>-0.395</td>
<td>-0.060</td>
<td>0.674</td>
<td>0.942</td>
<td>0.06</td>
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<tr>
<td>( \lambda_2 )</td>
<td>1.504</td>
<td>0.053</td>
<td>4.500</td>
<td>1.054</td>
<td>-0.462</td>
<td>-0.097</td>
<td>0.630</td>
<td>0.908</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>( \lambda_3 )</td>
<td>0.962</td>
<td>0.064</td>
<td>2.617</td>
<td>1.066</td>
<td>-0.598</td>
<td>-0.172</td>
<td>0.550</td>
<td>0.842</td>
<td>0.26</td>
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<td>( \lambda_4 )</td>
<td>0.513</td>
<td>0.133</td>
<td>1.670</td>
<td>1.142</td>
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<td>0.501</td>
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<td>-0.277</td>
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<td>1.133</td>
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<td>0.468</td>
<td>0.816</td>
<td>1.597</td>
<td>2.57</td>
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Table - 2 : Values of Activity and Activity-coefficient of components in binary alloy of OPD-IM system.
Table - 3 : Values of partial and integral thermodynamic mixing functions of alloys of OPD-IM system

<table>
<thead>
<tr>
<th>Alloy</th>
<th>$-\mu_{\text{OPD}}$ J/Mole</th>
<th>$-\mu_{\text{IM}}$ J/Mole</th>
<th>$-\mu_{\text{Total}}$ J/Mole</th>
<th>$h_{\text{OPD}}$ J/Mole/K</th>
<th>$h_{\text{IM}}$ J/Mole/K</th>
<th>$h_{\text{Total}}$ J/Mole/K</th>
<th>$s_{\text{OPD}}$ J/Mole/K</th>
<th>$s_{\text{IM}}$ J/Mole/K</th>
<th>$s_{\text{Total}}$ J/Mole/K</th>
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<td>A₁</td>
<td>-1169.115</td>
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<td>-237.079</td>
<td>23.390</td>
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Table - 4 : Values of partial and integral thermodynamic excess functions of alloys of OPD-IM system

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<tr>
<th>Alloy</th>
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<th>$\Delta g_{\text{IM}}$ J/Mole</th>
<th>$\Delta g_{\text{Total}}$ J/Mole</th>
<th>$\Delta h_{\text{OPD}}$ J/Mole</th>
<th>$\Delta h_{\text{IM}}$ J/Mole</th>
<th>$\Delta h_{\text{Total}}$ J/Mole</th>
<th>$\Delta s_{\text{OPD}}$ J/Mole/K</th>
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Fig. 1 Phase diagram of IM – OPD system

- Thaw temperature
- Melting temperature
Fig. 2 Graphical solution of activity of IM in binary mix

Fig. 3 Graphical solution of activity coefficient of IM in binary mix

Fig. 4 Graphical solution of partial molar heat of mixing of IM in binary mix

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