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Study of phase diagram, thermal stability and microstructures of nicotinamide based binary organic systems

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ABSTRACT

Phase diagrams of the binary systems of Nicotinamide (NA) with o-Nitroaniline (oNA), Cinnamic acid (CA) and 2-Methylimidazole (MIm) have been studied by thaw melt method. The result infers that all these mixtures are simple eutectic in nature. Eutectics (E) of NA-oNA, NA-CA and NA-MIm are formed at 65 ℃, 100 ℃ and 102 ℃ melting temperature, respectively and 0.780, 0.502 and 0.549 mole fraction of oNA, CA and MIm respectively. Heat of fusion (ΔH) of all the alloys and eutectics are also calculated with the help of mixture law. Thermodynamic stability in form of excess stability and ideal stability of the alloys of all systems are discussed in the present work. It gives an idea about the stability of eutectics and non-eutectics alloys of the systems. Interface morphology of the alloys predicts the faceted growth (α > 2) in all the cases in the light of Jackson's surface roughness (α) theory. The microstructures of pure components of taken binary systems having high entropy of fusion and its eutectics have also been discussed.

Keywords: Phase diagram, thermodynamic stability, roughness parameter, microstructure

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INTRODUCTION

The formation of organic molecular complexes by means of electronic theory of valency follows at ones in many cases from Sidwick's interpretation of Werner's theory. A number of different organic substances cannot be simply represented having their constituent molecules united by means of molecular rather than atomic forces; the union is in fact attributed to the action of the fields of the residual valency of either molecules or group of atoms. Physical as well as chemical forces are involved in the formation of eutectic and non-eutectic alloys. Thermochemical studies unfold the nature of mixing as well as nature of interaction between components during binary mix. Thermodynamics in materials science has often been used indirectly through phase diagrams. The science of growth has been developed on the foundation of thermodynamics, kinetics, fluid dynamics, crystal structures and interfacial sciences. The microstructure of a material has been found significantly important in deciding its mechanical, electrical, magnetic and optical properties. During solidification, various microstructures form in the alloys. While alloy properties are largely determined by the components used and the composition of the components, microstructure formed during solidification of alloy is also important in improving the properties. The creation of alloy microstructures causes a local change in the composition and this is the reason why alloy properties are influenced by the microstructures. Nicotinamide is water soluble aromatic organic component of vitamin B-complex group. In vivo, nicotinamide is incorporated into nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP) [1]. Nicam gel is most effective when applied to the skin, which helps to reduce the inflammation and redness of inflammatory acne [2]. The comprehensive review of nicotinamide's pharmaceutical effects came in light in 1991 as an anti HIV agent [3] and after that popularized vastly. Eutectic and non-eutectic solid dispersions [4, 5] of active pharmaceutical hydrophobic ingredients (APIs) with hydrophilic excipient Nicotinamide (NA) are important not only because of the ability to control pharmaceutical properties

without changing covalent bonds but also they can be used in the design [6] of new materials. In recent years, advances in supramolecular engineering and chemistry have motivated to extend research on the design of pharmaceutical materials by directing molecular association of different components in the crystalline state to form binary/ternary solid dispersions of potential interest. Pharmaceutical properties of some binary solid dispersion have also been reported [7, 8] by their enhanced solubility, dissolution rate, hygroscopicity, and chemical stability. Eutectic mixture formation between nicotinamide based drugs and hydrophilic carriers were investigated [9] recently to reduce the drug particle size, and increases the dissolution rate and thus changes the biopharmaceutical properties. The main objective of this paper is to introduce the quantitative link between phase diagrams and thermodynamic properties of Nicotinamide (NA) based binary organic systems with Cinnamic acid (CA), o-nitroaniline (oNA) and 2-methylimidazole (MIm). The solid-liquid equilibrium phase diagram, interfacial studies and investigation of microstructures of eutectic and non-eutectic alloys of all the systems are discussed.

EXPERIMENTAL SECTION

Nicotinamide (Thomas Baker, Bombey) and Cinnamic acid (G. S. Chemical, New Delhi) were purified by successive re-crystallization from boiling water while o-Nitroaniline (G. S. Chemical, New Delhi) and 2-Methylimidazole (G. S. Chemical, New Delhi) were directly taken for investigation. The melting point (experimental value) of nicotinamide, o-nitroaniline, cinnamic acid and 2-methylimidazole was found to be 128°C, 74°C, 132°C and 143°C, respectively. The solid-liquid equilibrium data of all system were determined by the Thaw-melt method [10, 11]. Mixtures of different composition were made in glass test tubes by repeated heating and followed by chilling in ice. The melting and thaw temperatures were determined in a Toshniwal melting point apparatus using a precision thermometer (± 0.1°C). The heater was regulated to rise in temperature by more than 1°C every five minutes.

To study the microstructure of the pure components and eutectics, a small sample was taken on a well washed and dried glass slide and placed in an oven maintained at a temperature slightly above the melting point of the sample. On complete melting a cover-slip was glided over the melt and allowed to cool. After a few minutes, the supercooled melt was nucleated by the solid of the same composition and care was taken to have unidirectional freezing [12]. After the complete freezing, the slide was placed on the platform of an SES, DMS-01, digital microscope where observation of the different regions of the slide was carried out.

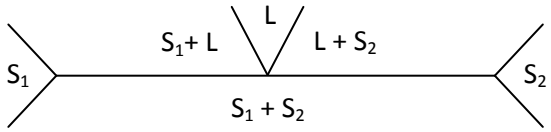
RESULTS AND DISCUSSION

Phase diagram (SLE) study

Thermodynamics in materials science has often been used indirectly through phase diagrams. The solid-liquid equilibria [13, 14] (SLE) data of NA –oNA, NA-CA and NA-MIm systems determined by the Thaw melt method is reported in the form of temperature-composition curve (Fig.1, 2 & 3). All systems show the formation of simple eutectic [15, 16]. The melting point of NA (128°C) decreases on the addition of second component and further attains minimum and then increases. At the eutectic temperature, two phases (a liquid phase L and two solid phases S_1 and S_2) are at equilibrium and

$$L \underset{\text{Cooling}}{\rightleftharpoons} S_1 + S_2$$

the system is invariant. The equilibrium involved among the phases are represented by the diagram

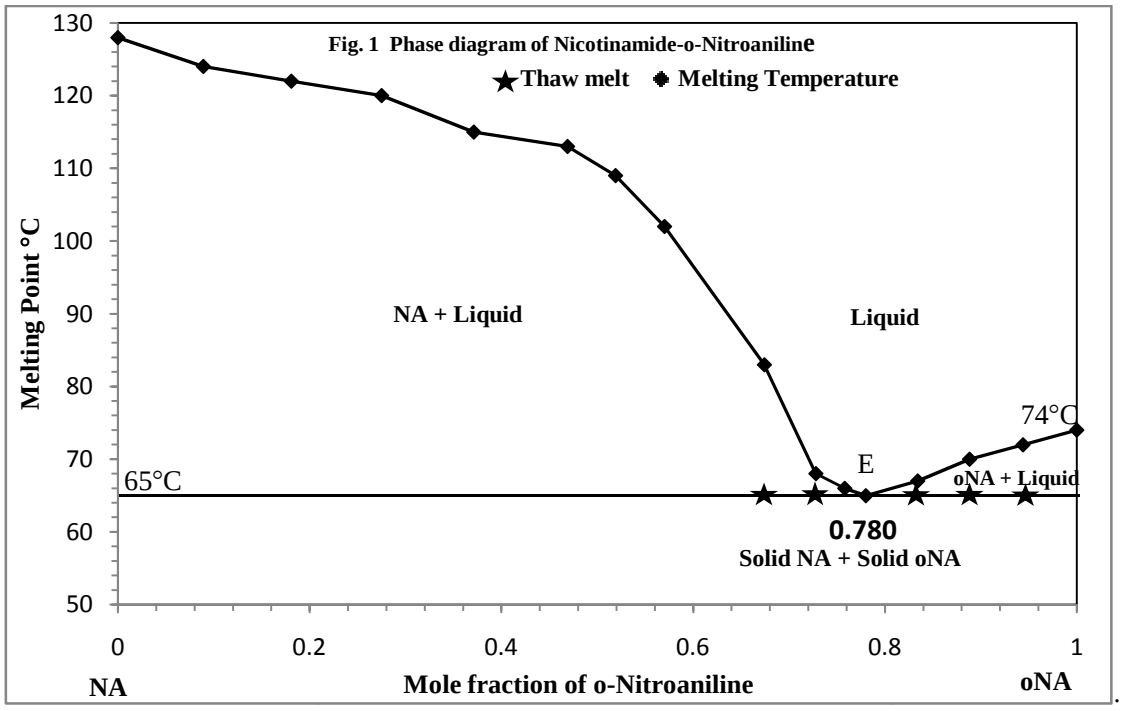


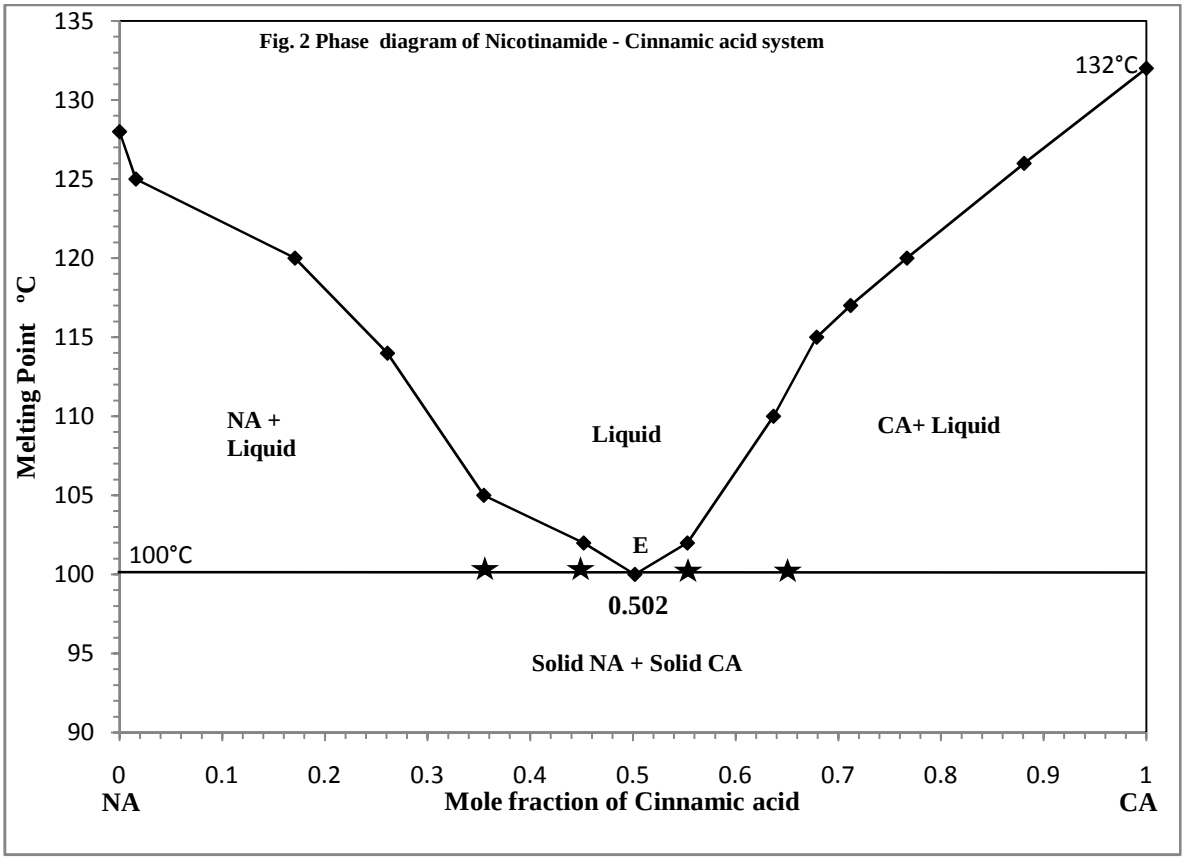
where in the eutectic region indicated by L a homogenous binary liquid solution exists, while the two solid phases exist below the horizontal line. In the case, in region located on the left side of the diagram a binary liquid and solid NA co-exist, while the region located on the right side of the diagram a binary liquid and second component co-exist equilibrium (note that S_1 is solid NA, while S_2 is solid second component).

The chemical interaction between two components in a binary system leads to an association of molecules in definite quantities. Physical as well as chemical forces are involved in the formation of eutectic and non-eutectic alloys. Thermochemical studies unfold the nature of mixing as well as nature of interactions between components of a binary mix.

Nicotinamide (NA) – o-Nitroaniline (oNA) System

The solid-liquid equilibrium data of NA-oNA system was determined by Thaw-melt method exhibit formation of a simple eutectic (Fig. 1) at 0.780 mole fraction of second component o-nitroaniline and at melting temperature 65°C.





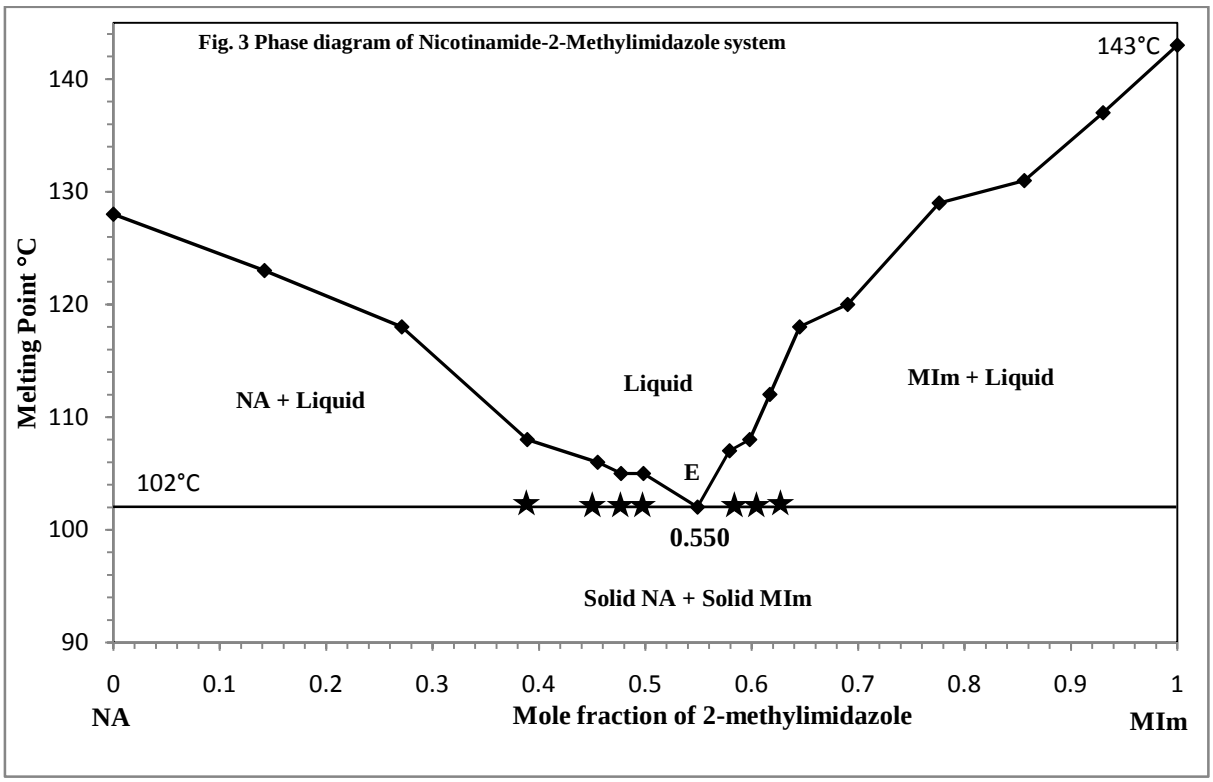
Nicotinamide (NA) – Cinnamic acid (CA) System

The solid-liquid phase diagram of NA-CA system shows simple eutectic shown in Fig. 2. Eutectic of NA-CA system is formed at 100°C and 0.502 mole fraction of Cinnamic acid. The chemical interaction between two components in

a binary system leads to an association of molecules in definite quantities. Physical as well as chemical forces are involved in the formation of eutectic and non-eutectic alloys.

Nicotinamide(NA) – 2-Methylimidazole(MIm) System

The solid-liquid equilibrium phase diagram of NA-MIm system determined by the thaw melt method is reported in the form of temperature-composition curve (Fig. 3) [17]. NA-MIm system shows the formation of simple eutectic. Eutectic of NA-MIm is formed at 102°C and 0.451 mole fraction of MIm.



Thermochemistry

The enthalpy of fusion of pure NA, oNA, CA and MIm are 25.40, 16.10, 23.14 and 12.67 kJ/mol, respectively. The enthalpy of fusion of eutectic (E) and non-eutectic alloys of all systems are calculated by the mixture law using equation [18]

$$(\Delta H)_e = \chi_{NA}\ \Delta H_{NA} + \chi_{oNA}\,\Delta H_{oNA} \qquad (1)$$

where χ and ΔH are the mole fraction and the heat of fusion of the component indicated by the subscript, respectively. The enthalpy of fusion values of binary alloys and eutectic (E) of all three systems taken are reported in Table 1.

The activity coefficient/activity of components for the systems has been calculated from the equation [19] given below

$$-ln\chi_i^1\gamma_i^1 = \frac{\Delta H_i}{R}\left(\frac{1}{T_e} - \frac{1}{T_i}\right) \qquad (2)$$

$$a_i = \chi_i\gamma_I \qquad (3)$$

where a_i and γ_i^1 is activity and activity coefficient of the component *i* in the liquid phase respectively, ΔH_i is the heat of fusion of component i at melting point T_i and R is the gas constant. T_e is the melting temperature of alloy.

Using the values of activity and activity coefficient (Table 1) of the components in alloys stability, excess stability and ideal stability have been computed.

Table 1. Phase composition, melting point, enthalpy of fusion values, roughness parameter

Alloy	χ_i ($i = 2^{nd}$ component)	MP (°C)	ΔH (kJ/mol)	α	a_i	γ_i
NA-oNA system						
A1	0.944	72	16.62	5.79	0.97	1.03
A2	0.888	70	17.14	6.01	0.94	1.06
A3	0.834	67	17.64	6.24	0.89	1.07
E	0.780	65	18.15	6.46	0.86	1.10
A4	0.758	66	18.35	6.51	0.88	1.16
A5	0.728	68	18.63	6.57	0.91	1.25
A6	0.674	83	19.13	6.46	1.15	1.71
A7	0.570	102	20.10	6.45	1.52	2.66
A8	0.519	109	20.57	6.48	1.67	3.21
A9	0.469	113	21.04	6.56	1.76	3.75
A10	0.371	115	21.95	6.80	1.80	4.86
A11	0.275	120	22.84	6.99	1.92	6.99
A12	0.181	122	23.72	7.22	1.97	10.89
A13	0.089	125	24.57	7.43	2.04	22.97
NA-CA System						
A1	0.881	126	23.41	7.06	0.76	0.87
A2	0.767	120	23.67	7.24	0.69	0.90
A3	0.712	117	23.79	7.34	0.65	0.91
A4	0.679	115	23.87	7.40	0.63	0.92
A5	0.658	111	23.91	7.49	0.58	0.88
A6	0.637	110	23.96	7.52	0.57	0.90
A7	0.553	102	24.15	7.75	0.49	0.88
E	0.502	100	24.27	7.82	0.47	0.94
A8	0.452	102	24.38	7.82	0.49	1.08
A9	0.355	105	24.60	7.83	0.52	1.46
A10	0.261	114	24.81	7.71	0.62	2.36
A11	0.171	120	25.01	7.66	0.69	4.02
A12	0.016	125	25.36	7.67	0.75	46.93
NA-MIm System						
A1	0.930	137	13.56	3.98	1.05	1.13
A2	0.856	131	14.50	4.32	0.99	1.16
A3	0.776	129	15.52	4.64	0.97	1.25
A4	0.690	120	16.62	5.09	0.89	1.29
A5	0.645	118	17.19	5.29	0.87	1.36
A6	0.617	112	17.55	5.48	0.82	1.33
A7	0.598	108	17.79	5.62	0.79	1.32
A8	0.579	107	18.03	5.71	0.78	1.35
E	0.549	102	18.41	5.91	0.74	1.35
A9	0.498	105	19.06	6.07	0.76	1.54
A10	0.477	105	19.33	6.15	0.76	1.60
A11	0.455	106	19.61	6.22	0.77	1.70
A12	0.389	108	20.45	6.46	0.79	2.03
A13	0.271	118	21.95	6.75	0.87	3.23
A14	0.142	123	23.59	7.17	0.92	6.47

Stability Functions

Thermodynamic strength of the present system in form of stability and excess stability functions [20, 21] can be determined by the second derivative of their molar free energy and excess energy respectively, with respect to the mole fraction of either constituent:

$$Stability = \frac{\partial^2 \Delta G^M}{\partial \chi^2} = -2RT \frac{\partial \ln a}{\partial (1-\chi)^2} \quad (4)$$

$$Excess\ Stability = \frac{\partial^2 g^E}{\partial \chi^2} = -2RT \frac{\partial \ln \gamma}{\partial (1-\chi)^2} \quad (5)$$

These values may be calculated by multiplying the slope of lna vs $(1 - \chi)^2$ and lnγ vs $(1 - \chi)^2$ plots with -2RT. The values of total stability to the ideal stability and defined as

$$Ideal\ Stability = \frac{RT}{\chi(1-\chi)} \qquad (6)$$

These values show the overall thermodynamic stability in the alloy. It is evident from the Figs. 4-6, that the negative value of stability, excess stability and ideal stability of binary alloys, predicts the stronger stabilization in the binary alloys. Values of stability, excess stability and ideal stability of eutectics of all systems are given in Table 2 and also eutectics and non-eutectics alloys are shown in figs 4-6 in the form of graph.

Table 2. Values of Stability, Excess stability and Ideal stability of Binary System

Eutectic of Alloys	Stability (J/mol)	Excess Stability (J/mol)	Ideal Stability (J/mol)
NA – oNA System	5620.26	-9385.84	16376.06
NA – CA System	-3101.12	-15505.61	12404.69
NA – MIm System	-6235.50	-20764.22	12591.93

Fig. 4 Stability Function of NA-oNA System

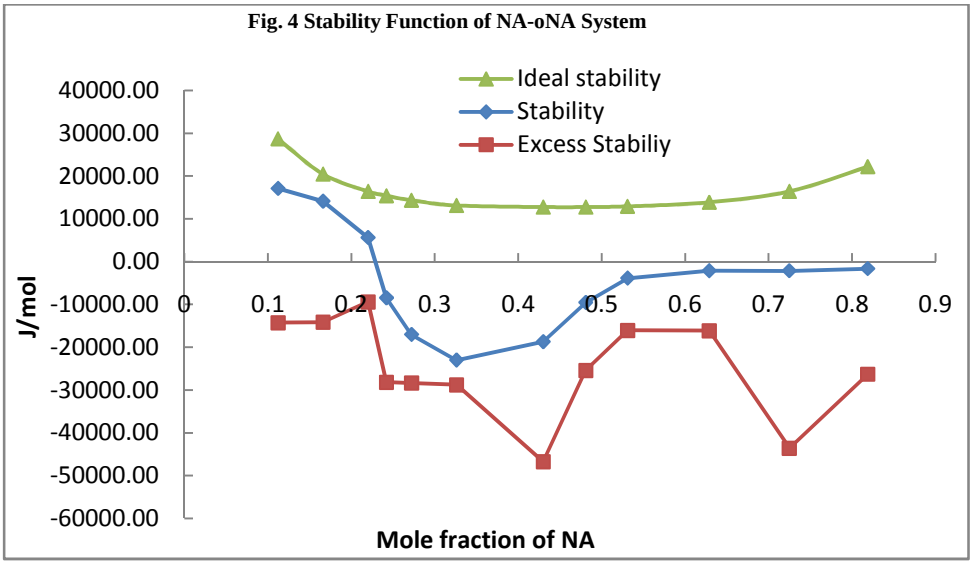
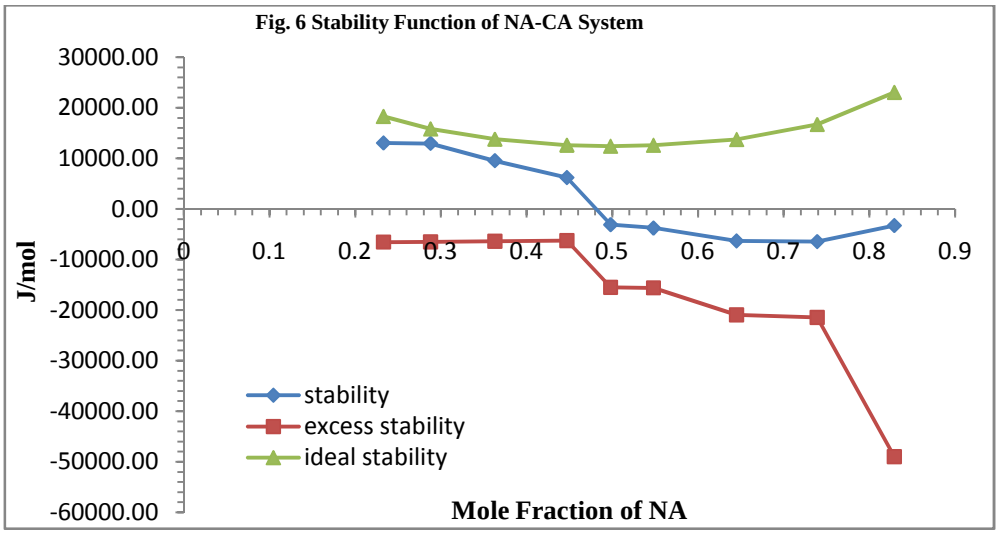
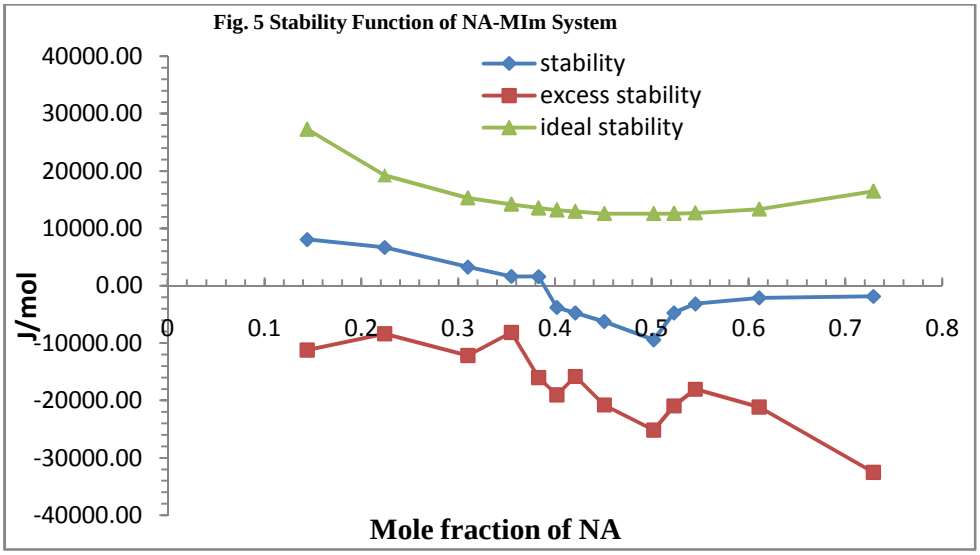


Fig. 6 Stability Function of NA-CA System





Microstructure of pure components and eutectic

It is well known that in polyphase materials the microstructure gives the information about shape and size of the crystals and it is important in deciding its mechanical, electrical, magnetic and optical properties of material. The science of growth has been developed on the foundation of thermodynamics, kinetics, fluid dynamics, crystal structures and interfacial sciences. The solid-liquid interface morphology can be predicted from the value of the entropy of fusion. According to Hunt and Jackson [22], the type of growth from a binary melt depends upon a factor α, defined as:

$$\alpha = \xi \frac{\Delta H}{RT} = \xi \frac{\Delta S}{R} \qquad (7)$$

where ξ is a crystallographic factor depending upon the geometry of the molecules and has a value less than or equal to one. ΔS/R (also known as Jackson's roughness parameter α) is the entropy of fusion (dimensionless) and R is the gas constant. When α is less than two the solid-liquid interface is atomically rough and exhibits non-faceted growth. The value of Jackson's roughness parameter (ΔS/R) is given in Table 1. The computed α values of pure NA, oNA, CA and MIm are of the order of 7.62, 5.58, 6.71 and 3.76, respectively revealing the faceted morphology of the binary composite material. For the entire alloy of all the systems, the α values [23] were found to be greater than 2 which indicate the faceted growth proceeds in all the cases.

The microstructure of pure components NA, oNA, CA and MIm and its eutectics are shown in Fig. 7-13. The microstructure obtained for the eutectics are of thinly branched, interdendritic, complex regular and irregular type whereas the microstructure obtained for components are of complex and irregular type. A prediction of microstructure [24] (given in Table 3) of eutectics can be made from Spengler's equation [25].

$$\theta = \frac{T_1 - T_E}{T_2 - T_E} \qquad (8)$$

where T_1 and T_2 are the melting temperature of low melting and high melting components, respectively, while T_E is the eutectic temperature. Normal eutectics are formed as θ lies between 0.1 and 1.0. However, a value between 0.01 and 0.1 indicates anomalous structure, while a divorced structure prelives for θ less than 0.01. According to Podolinsky et al. [26], the surface roughness factor of one component increases or decreases under the influence of another component in a binary eutectic, as a result which the structure of eutectic becomes regular. The α factor of either eutectic phase decreases under the influence of having components of opposite eutectic phases, where anomalous eutectics can be formed. The microstructure of eutectic NA-oNA system having 0.780 mole fraction of second component shows a sharp radial growth (Fig. 11) from the nucleating centre. The nodules of low melting constituent phase is being radiated outward from the centre of other eutectic phase and grows normal to solidification interface. The microstructure of eutectic of NA-CA system (Fig. 12) containing 0.502 mole fraction of CA shows conglomerate morphology. It is formed as a result of separate growth of eutectic phases. In this morphology there is co-existence of eutectic phases in a particular region. This may be due to difference of

undercooling and growth rate of the phases and leading of one of phases followed by other phase in the eutectic. The microstructure of eutectic of NA-MIm system containing 0.549 mole fraction of MIm (Fig. 13) shows complex regular morphology. It is observed as a result of an energy barrier that exists for the addition of new solid layer during solidification which proceeds by the lateral movement of steps across a specific crystallographic facet plane.

Table 3. Computed and observed microstructure of eutectics

System	θ	Computed Microstructure	Observed Microstructure
8. NA – oNA System Eutectic	0.143	Regular	Sharp radial growth
4. NA – CA System Eutectic	0.875	Regular	Conglomerate
6. NA – MIm System Eutectic	0.634	Regular	Complex regular

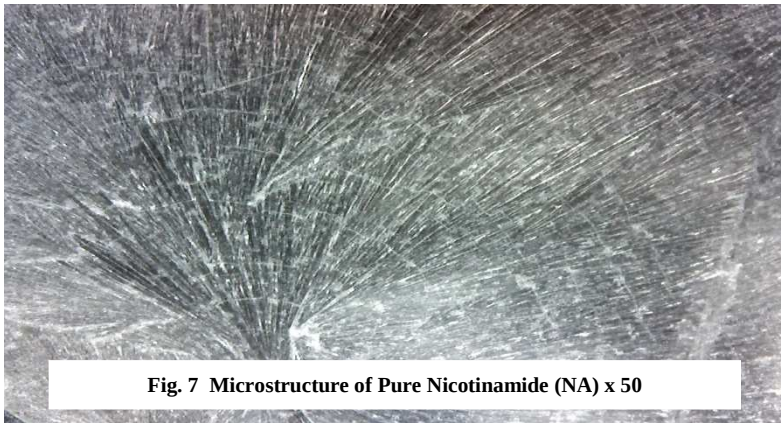


Fig. 7 Microstructure of Pure Nicotinamide (NA) x 50

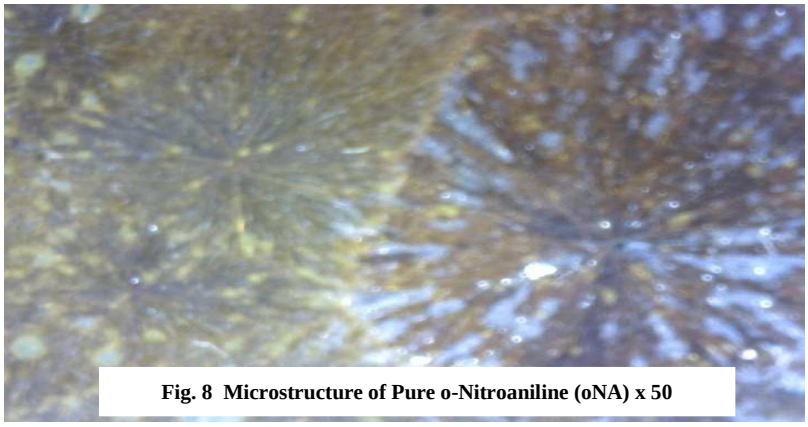


Fig. 8 Microstructure of Pure o-Nitroaniline (oNA) x 50

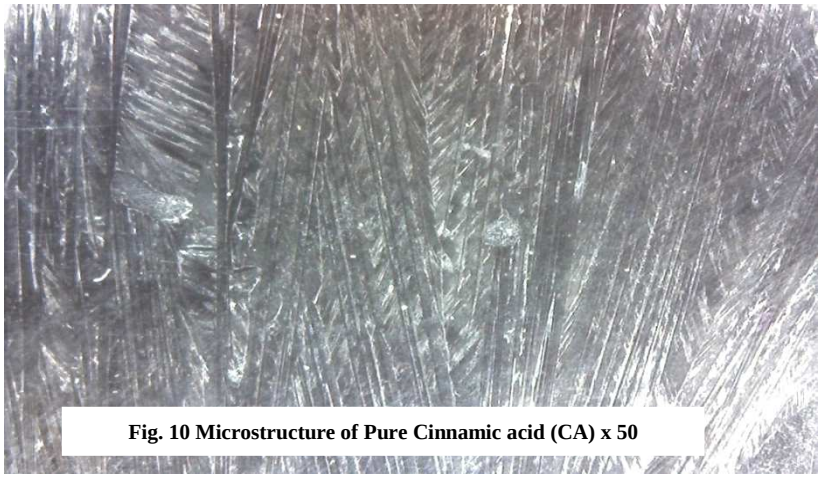


Fig. 10 Microstructure of Pure Cinnamic acid (CA) x 50

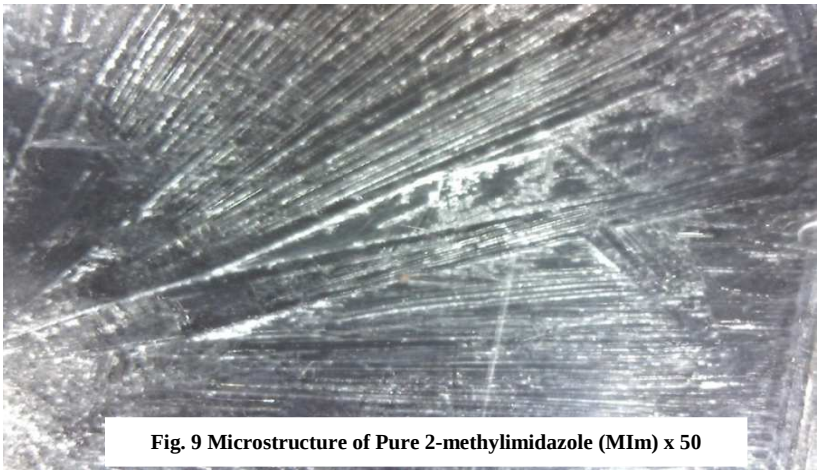


Fig. 9 Microstructure of Pure 2-methylimidazole (MIm) x 50

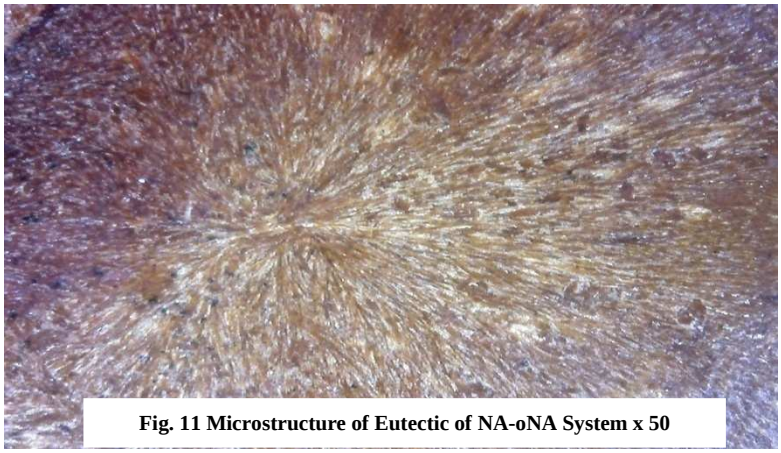


Fig. 11 Microstructure of Eutectic of NA-oNA System x 50

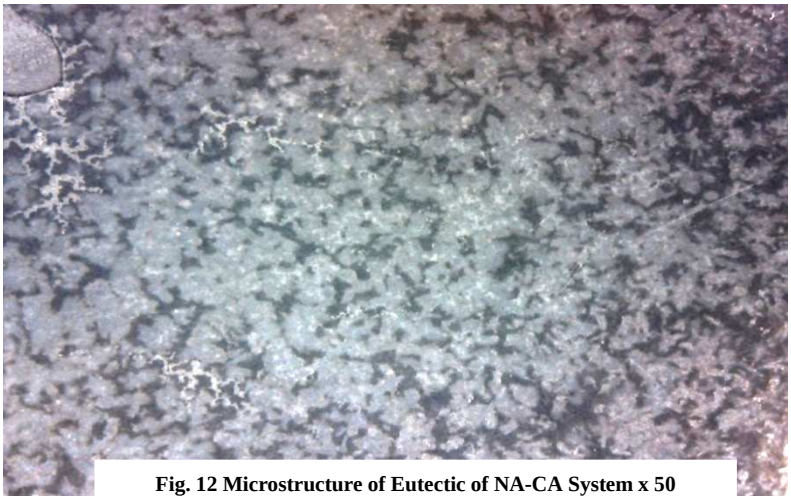


Fig. 12 Microstructure of Eutectic of NA-CA System x 50

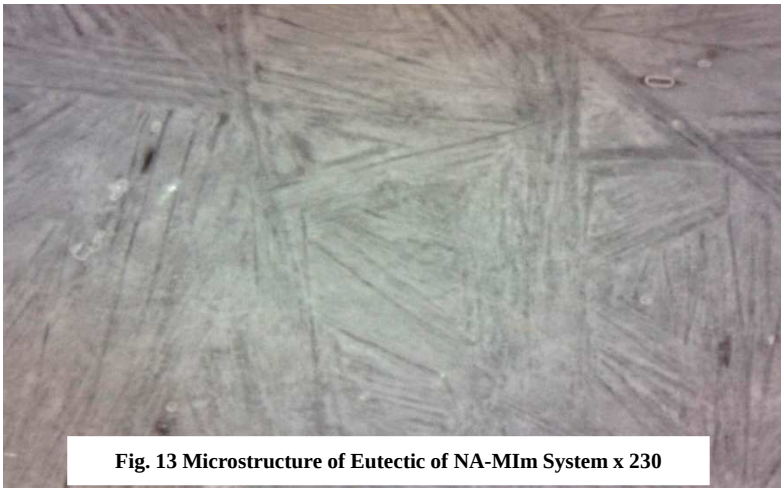


Fig. 13 Microstructure of Eutectic of NA-MIm System x 230

CONCLUSION

The solid-liquid equilibria of the systems NA-oNA infer the formation of simple eutectic. Jackson's Interface roughness ($\alpha > 2$) predicts the faceted growth leads in all the eutectic and non-eutectic alloys. The negative value of stability, excess stability and ideal stability of binary alloys predicts the stronger stabilization in the binary alloys. The microstructure of eutectic of NA-oNA shows a sharp radial growth from the nucleating centre, microstructure of NA-CA shows conglomerate morphology while microstructure of eutectic of NA-MIm shows complex regular morphology.

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