



STUDY OF PHASE DIAGRAM AND MICROSTRUCTURES OF SOME NICOTINAMIDE BASED BINARY ORGANIC EUTECTIC

VISHNU KANT

Department of Chemistry, V.K.S. University, Ara, Bihar, India



Vishnu Kant

Article Info:

Received: 04/08/2013

Revised from:11/08/2013

Accepted on:12/08/2013

ABSTRACT

Phase diagram of binary organic alloys of Nicotinamide(NA) with Vanillin(VA), Acetanilide(ACT), β -Naphthol(β N) and Benzamide(BZ) have been determined by Thaw-melt method which suggests the formation of simple eutectic in all cases. Eutectic E of NA-ACT, NA- β N and NA-BZ system achieved at MP 93°C, 65°C and 105°C respectively and mole fractions 0.598, 0.611 at 0.391 of ACT, β N and BZ respectively. NA-VA system shows the formation of a eutectic with two incongruently/non-congruently melting 3:2 at 100°C and 1:2 at 90°C addition compounds respectively. Heat of fusion (ΔH) of all the alloys and eutectics are also calculated with the help of mixture law. Interface morphology of the alloys follows the Jackson's surface roughness (α) theory and predicts the faceted growth proceeds in all the alloys. The microstructure of pure components of taken binary systems having high entropy of fusion as well as the binary organic eutectics of NA-VA, NA-ACT, NA- β N and NA-BZ has been discussed in the present investigation.

Keywords:- Phase diagram, Heat of fusion, Surface roughness, Microstructure

INTRODUCTION

Formation of molecular complexes of an organic compound with other compounds is due to molecular interactions between them. It is important because the ability to control physical, chemical and pharmaceutical [1,2] properties without changing the parent covalent bonds. In recent years, research work may extend on the design of pharmaceutical materials [3] by directing molecular association of different components in the solid state to form binary/ternary materials of potential interest. The interface is understood as boundary between liquid and the solid. It is normally described as smooth when the boundary is discrete and rough when the transition extends over a number of atomic layers. The simplest approach for defining the structure of interface during phase transformation is based on atomic/molecular scale, consideration of atomic/molecular motion, available surface site and sites occupied on interface, driving force of transformation and finally the value of surface roughness parameter (α). The microstructure of a material

has been found significantly important in deciding its mechanical, electrical, magnetic and optical properties.

Nicotinamide(NA) is a water soluble component of the vitamin B complex group. In vivo, nicotinamide is incorporated into nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP). The physiological function and pharmaceutical action of NAD and NADP is to function as enzymes in a wide variety of enzymatic oxidation-reduction reactions essential for tissue respiration, lipid metabolism and glycogenolysis. It is anti HIV [4], anti M. tuberculosis [5], anti inflammatory [6] and anti Pellagra [7] agent. Nicam gel [8] is most effective when applied to the skin, which helps to reduce the inflammation and redness of inflammatory acne. Vanillin (VA) is used in flavorings, fragrances, pharmaceuticals, and perfumes. It is also used as a potential agent for the treatment of Sickle Cell Anemia [9], a Blood disorder. The psychotherapeutic use of vanillin encompasses as an anti-anxiety agent [10], an anticonvulsant, and/or as a sedative (sleeping drug). Acetanilide is extensively used as antipyretic and analgesic

agents. β -Naphthol is employed in pharmaceutical, agricultural and rubber industries. Keeping this view in mind nicotinamide (NA) is used as basic material for synthesis of its binary organic alloys. In the present piece of my investigation of Nicotinamide(NA) with Vanillin(VA), Acetanilide (ACT), β -Naphthol(β N) and Benzamide(BZ) binary organic systems has been taken for detailed studies such as, phase diagram, interfacial roughness and microstructures of eutectic and non-eutectic alloys.

EXPERIMENTAL DETAILS

Nicotinamide (Thomas Baker, Bombay), was directly taken for investigation. Vanilline (G. S. Chemical, New Delhi) were purified by successive recrystallization from boiling water while Acetanilide (Qualigen, Fine Chemicals, Bombay) was purified by slow sublimation method followed by repeated distillation under vacuum method. β -Naphthol (E. Merck, Bombay) was purified by recrystallization from boiling ethanol. Benzamide (G. S. Chemical, New Delhi) was purified by successive distillation from ethanol under reduced pressure. 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 which could read correctly up to $\pm 0.1^\circ\text{C}$. The heater was regulated to give above 1°C increase in temperature in every five minutes. The experimental value of melting point of NA, VA, ACT, β N and BZ are 128°C , 84°C , 119°C and 123°C , respectively. The solid-liquid equilibrium data of all the systems were measured by the Thaw-melt method [11,12].

Heat of fusion of materials were measured by the DTA method [13,14] using NETZSCH Simultaneous Thermal Analyzer, STA 409 series unit. All the runs were carried out with heating rate $2^\circ\text{C}/\text{min}$, chart speed $10\text{mm}/\text{min}$ and chart sensitivity $100\mu\text{v}/10\text{mv}$. The sample weight was 5 mg for all estimation. Using benzoic acid was a standard substance, the heat of fusion of unknown compound was determined using the following equation:

$$\Delta H_x = \frac{\Delta H_s W_s A_x}{W_x A_s} \quad (1)$$

where ΔH_x is the heat of fusion of unknown sample and ΔH_s is the heat of fusion of standard substance. W and A are weight and peak area, respectively and suffices x and s

indicate the corresponding quantities for the unknown and standard substances, respectively.

To study the microstructure of the pure components and eutectics, a small amount of 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 super cooled melt was nucleated by the solid of the same composition and care was taken to have unidirectional freezing [15]. After the complete freezing, the slide was placed on the platform of a SES, DMS-01, digital microscope and the different regions of the slide were carried out.

RESULT AND DISCUSSION

PHASE DIAGRAM

Phase diagram of all the systems exhibits the formation of simple eutectic [16–19]. In case on addition of one component into second, the melting point of second decreases and attains a minimum which is the eutectic temperature of the system. The maximum value of under cooling of parent components being of the same order in system suggests that any of the components can nucleate first during solidification. The eutectic compositions (E) and the corresponding temperature are reported in Table. At the eutectic temperature both components separate out from the liquid phase at a constant composition, until the entire liquid phase disappears, here, the solution E is either saturated or is in equilibrium with both the solid phases and the system is invariant. At the eutectic temperature the composition of the solid is the same as that of the liquid from which it separates. If any attempt is made to cool the liquid below the eutectic temperature (T_E), it will cool only if one phase is vanished.

Nicotinamide (NA) – Vanillin (VA) System

The data for fused mixtures of the present NA-VA system were obtained by Thaw-melt method which shows the formation of simple eutectic at 76°C and 0.820 mole fraction of vanillin. The phase diagram in temperature composition curve has been shown in Fig 1. The system shows the formation of a eutectic with two incongruently/non-congruently melting 3:2 at 100°C and 1:2 at 90°C addition compounds respectively. The compositions and their corresponding temperatures of eutectics and addition compounds of the systems undertaken are mentioned in Table 1.

Table1: Phase composition, Melting temperature, Values of Enthalpy of fusion and Roughness parameter

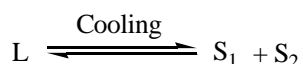
Alloys	χ_{NA}	χ_i	MP(°C)	$\Delta H(J/mol)$	α
NA – VA System					
A1	0.062	0.938	81	19884.56	6.76
A2	0.098	0.902	79	20096.24	6.87
A3	0.145	0.855	78	20372.60	6.98
E	0.18	0.82	76	20578.40	7.09
A4	0.237	0.763	88	20913.56	6.97
A5	0.348	0.652	90	21566.24	7.15
A6	0.454	0.546	96	22189.52	7.23
A7	0.555	0.445	99	22783.40	7.37
A8	0.604	0.396	100	23071.52	7.44
A9	0.651	0.349	111	23347.88	7.31
A10	0.744	0.256	120	23894.72	7.31
A11	0.833	0.167	122	24418.04	7.44
A12	0.918	0.082	127	24917.84	7.49
NA – ACT System					
A1	0.110	0.891	106	20270.72	6.43
A2	0.217	0.783	99	20888.65	6.75
A3	0.322	0.678	97	21492.85	6.99
A4	0.373	0.627	95	21790.90	7.12
E	0.402	0.598	93	21953.79	7.21
A5	0.424	0.576	95	22084.99	7.22
A6	0.475	0.525	98	22377.38	7.25
A7	0.525	0.475	100	22665.96	7.31
A8	0.624	0.376	106	23234.87	7.37
A9	0.721	0.279	113	23792.50	7.41
A10	0.816	0.184	116	24338.37	7.53
A11	0.909	0.091	122	24874.49	7.57
NA - β N System					
A1	0.116	0.884	110	18425.24	5.79
A2	0.228	0.772	91	19308.92	6.38
A3	0.336	0.664	75	20161.04	6.97
A4	0.357	0.643	71	20326.73	7.11
E	0.389	0.611	65	20579.21	7.32
A5	0.420	0.580	68	20823.80	7.35
A6	0.440	0.560	71	20981.60	7.34
A7	0.491	0.509	74	21383.99	7.41
A8	0.541	0.459	81	21778.49	7.40
A9	0.639	0.361	98	22551.71	7.31
A10	0.734	0.266	106	23301.26	7.39
A11	0.825	0.175	115	24019.25	7.45
A12	0.914	0.086	120	24721.46	7.57
NA – BZ System					
A1	0.104	0.896	126	23518.40	7.09
A2	0.207	0.793	121	23734.70	7.25
A3	0.308	0.692	116	23946.80	7.40
A4	0.410	0.590	112	24161.00	7.55
A5	0.510	0.490	108	24371.00	7.69
A6	0.560	0.440	106	24476.00	7.77
E	0.609	0.391	105	24578.90	7.82
A7	0.660	0.340	107	24686.00	7.81
A8	0.708	0.292	113	24786.80	7.72
A9	0.757	0.243	118	24889.70	7.66
A10	0.806	0.194	122	24992.60	7.61
A11	0.904	0.096	125	25198.40	7.62

Nicotinamide (NA) – Acetanilide (ACT) System

The temperature-composition curve of NA-ACT system shows the formation of simple eutectic at 0.598 mole fraction of acetanilide at 93°C which is shown in Fig. 2. The phase diagram of NA-ACT system was determined by the Thaw melt method. The melting point of NA (128°C) decreases on the addition of second component ACT (MP, 116°C) and further attains minimum and then increases.

Nicotinamide (NA) – β -Naphthol (β N) System

Solid-liquid equilibrium data of NA- β N system were obtained by Thaw-melt method and reported the formation of a simple eutectic at melting temperature 65°C and mole fraction of β -Naphthol is 0.611. The phase diagram of NA- β N system is shown in Fig. 3. The melting point of NA (128°C) decreases on the addition of second component β N (119°C) and further attains minimum and then increases. At the eutectic temperature two phases namely a liquid phase L and two solid phases (S_1 and S_2) are in equilibrium and the system is invariant. In the 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 exist while in a similar region located on the right side of the diagram, a binary liquid and the second component of the system co-exist.



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. The phase diagram of binary system forming simple eutectic follows the same mechanism.

Nicotinamide (NA) – Benzamide (BZ) System

The phase diagram [20] of the system shows the formation of simple eutectic at 0.391 mole fraction of BZ at the eutectic point, 105°C. Solid-liquid equilibrium data of the fused mixtures were obtained by Thaw-melt method. The temperature-composition curve of the system is shown in Fig. 4.

HEAT OF FUSION

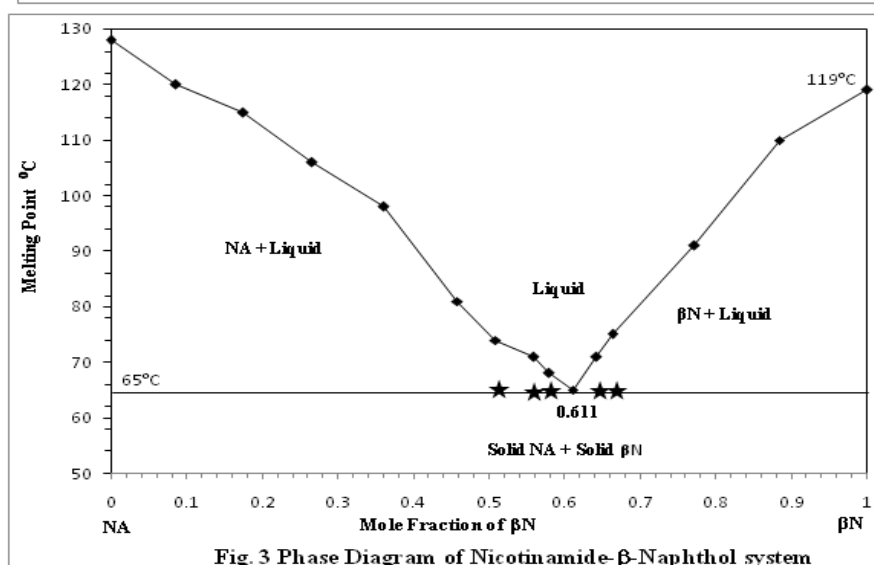
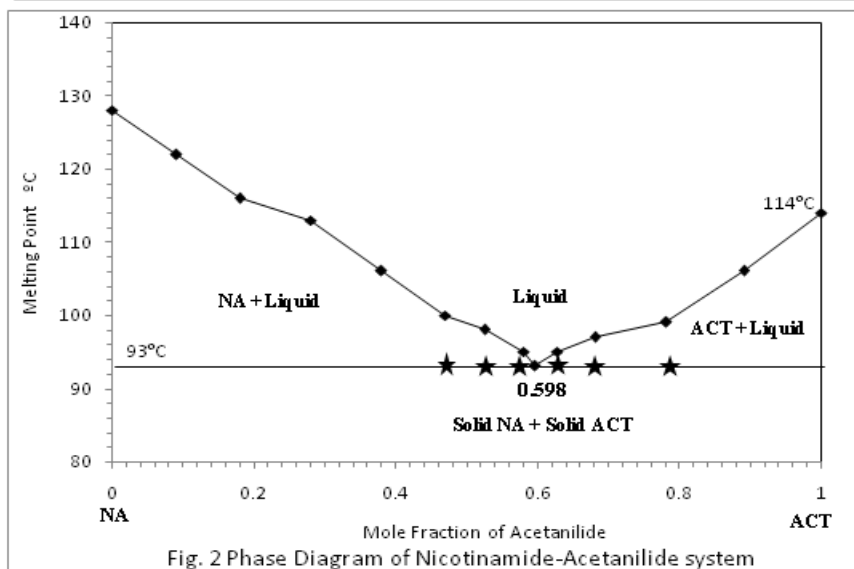
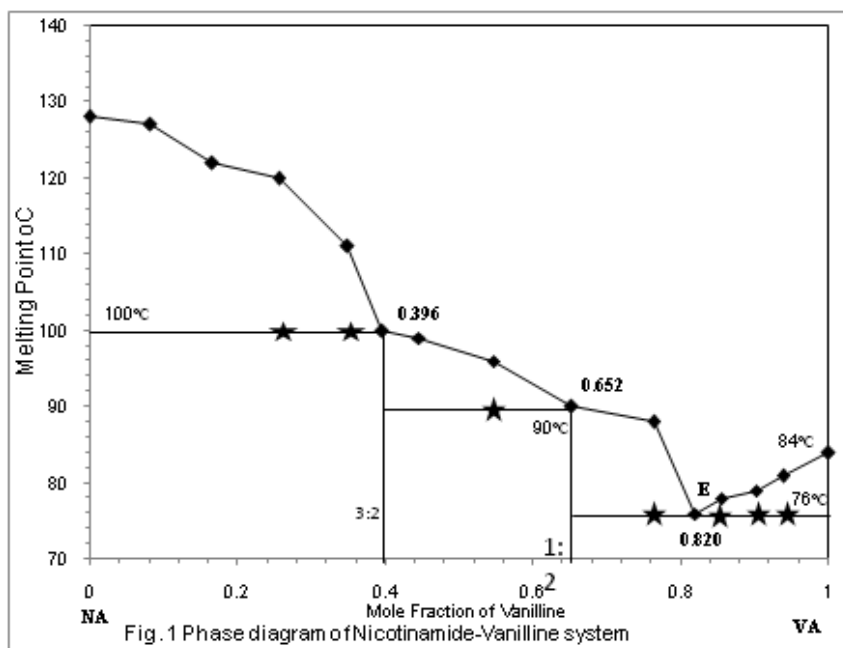
A eutectic alloy is recognized not to be a simple mechanical mixture of the components. The values of heat of fusion [21] of eutectic and non-eutectic solid dispersions are calculated by the mixture law using equation

$$(\Delta H)_e = \chi_{NA} \Delta H_{NA} + \chi_{VA} \Delta H_{VA} \quad (2)$$

where χ and ΔH are the mole fraction and the heat of fusion of the component indicated by the subscript, respectively. Heat of fusion of pure nicotinamide, vanillin, acetanilide, β -naphthol and benzamide are 25400, 19520, 19640, 17510 and 19500 J/mol respectively. The value of heat of fusion of eutectics and non-eutectic alloys of all the systems are reported in Table 1.

Table 2: Computed and observed microstructure of eutectics

System	θ	Computed Microstructure	Observed Microstructure
NA – VA System			
Eutectic	0.154	Regular	Spheruletic
NA – ACT System			
Eutectic	0.600	Regular	Irregular
NA – β N System			
Eutectic	0.857	Regular	Conglomerate
NA – BZ System			
Eutectic	0.957	Regular	Conglomerate



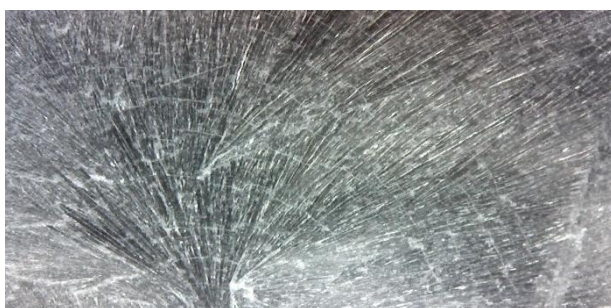
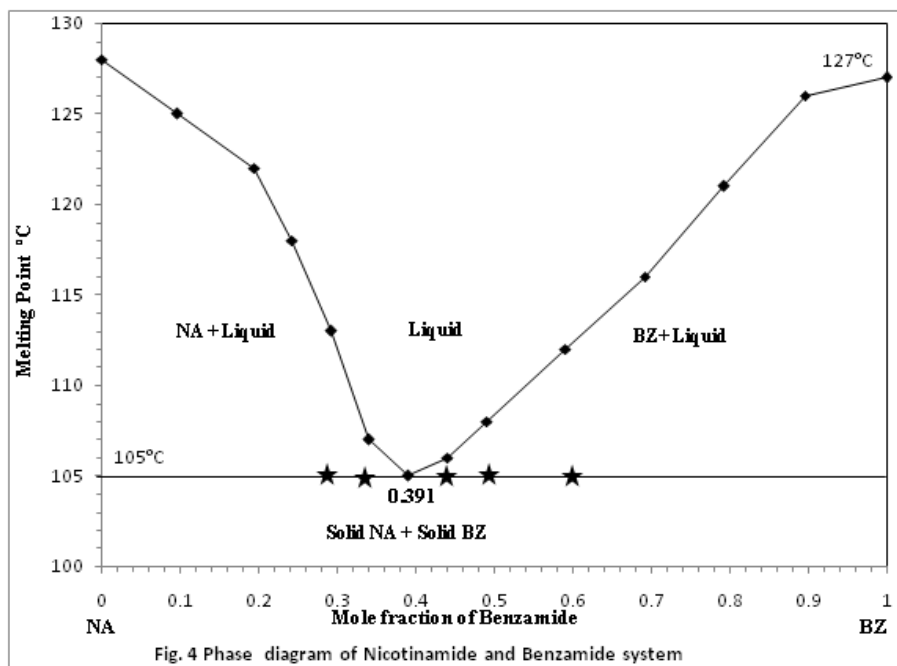


Fig. 5 Microstructure of Pure Nicotinamide (NA) x 50



Fig. 6 Microstructure of Pure Vanillin (VA) x 50

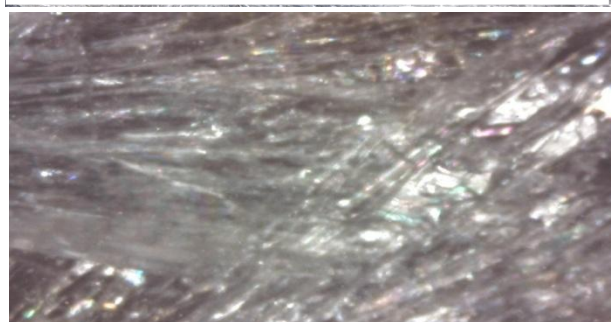


Fig. 7 Microstructure of Pure Acetanilide (ACT) x 230

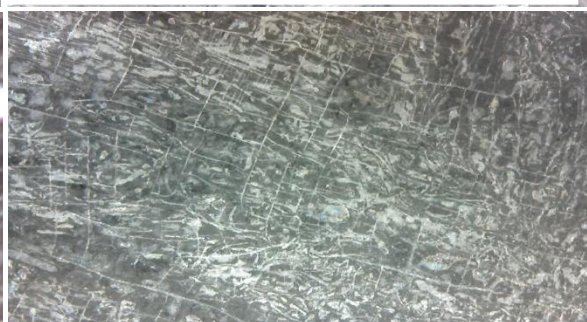


Fig. 8 Microstructure of Pure beta-Naphthol (BN) x 50

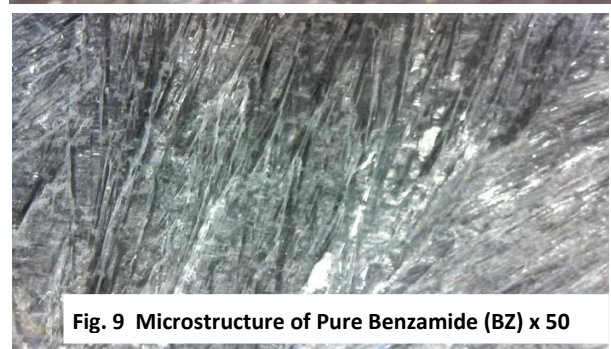


Fig. 9 Microstructure of Pure Benzamide (BZ) x 50

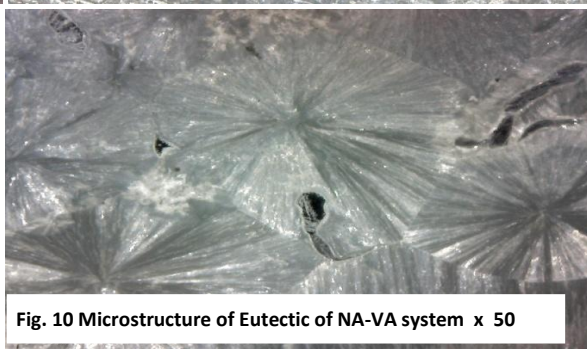


Fig. 10 Microstructure of Eutectic of NA-VA system x 50



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

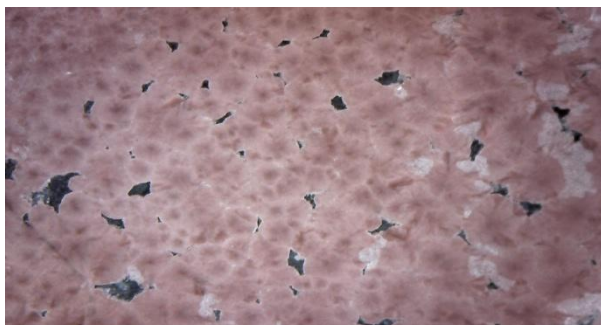


Fig. 12 Microstructure of Eutectic of NA-βN System x 50

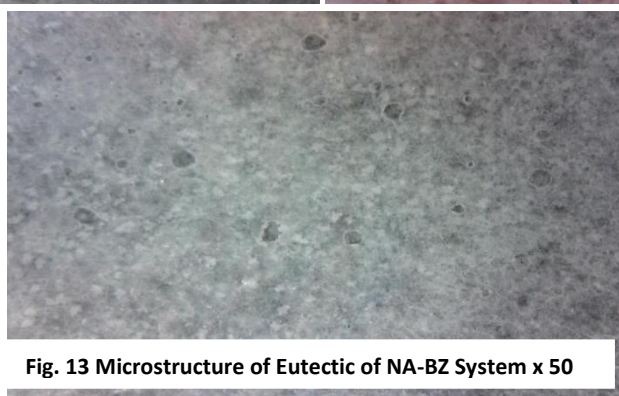


Fig. 13 Microstructure of Eutectic of NA-BZ System x 50

INTERFACE MORPHOLOGY

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 which is almost the entropy of fusion in dimensionless unit, defined precisely:

$$\alpha = \xi \frac{\Delta H}{RT} = \xi \frac{\Delta S}{R} \quad (3)$$

where $\xi \{T_d/T = (T - \Delta T)/T\}$ is a crystallographic factor depending upon the geometry of the molecules and has a value less than or equal to one. ΔS is the entropy of fusion and R is the gas constant. Irregular interface appears when $\alpha > 2$ for both phases, which concurrently initiate the anisotropic growth with crystalline facets. The nonfaceted crystal holds a round growth front while the faceted crystals possess a sharp growth front. The computed α values of pure NA, VA, ACT, βN and BZ respectively are of the order of 7.62, 6.58, 6.10, 5.37 and 7.01 revealing the faceted morphology of the binary composite material. The liquid-solid growth of the overall binary products due to their high entropies of fusion are greatly influenced by thermal and mechanical stresses and splitted into groups of crystals that gives rise to a regular morphology. The values of Jackson's roughness parameter ($\Delta S/R$) are given in Table 1. For all the alloys the α value was found greater

than 2 which indicate the faceted [23] growth proceeds in all the cases.

MICROSTRUCTURES OF PARENT COMPONENTS AND EUTECTICS

The microstructure of pure components and simple eutectics are shown in figs. 5-13. 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 of eutectics can be made from Spengler's equation [24]

$$\theta = \frac{T_1 - T_E}{T_2 - T_E} \quad (4)$$

where, T_1 and T_2 are the melting temperature of low melting and high melting components, respectively; and T_E is the eutectic temperature. The normal eutectics are formed when θ lies between 0.1 and 1.0 but it lies between 0.01 to 0.1 anomalous structure are obtained and when it acquires values less than 0.01, divorced structure are formed. The θ values of the eutectics of all the alloys are given in Table 2. According to Podolinsky [25] et. al. the surface roughness factor of one component increases or decreases under influence of another component in a binary eutectic, the regular eutectic structure is formed whereas α factor of both eutectic phases decreases under

the influence of the components of opposite eutectic phases, anomalous eutectics can be formed.

The microstructure of eutectic of NA-VA (Fig.10) system having 0.820 mole fraction of second component shows the spherule morphology. It appears due to abrupt and large undercooling and high melting temperature differences of two components while eutectic of NA- ACT (Fig. 11) system containing 0.598 mole fraction of second component exhibit irregular morphology in which the primary arm of a component grows a head of the eutectic interface and interspersed on second phase which is bounded by closed packed plane. The microstructures of eutectic of NA-βN and NA-BZ systems (Figs. 12, 13, respectively) containing 0.611, 0.391 mole fraction of second components 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.

CONCLUSION

The phase diagram of binary organic alloys of all the systems are found to be simple eutectic but NA-VA system shows the formation of a eutectic with two incongruently/non-congruently melting 3:2 at 100°C and 1:2 at 90°C addition compounds respectively. For all the alloys in all the binary systems the α value was found greater than 2 which indicate the faceted growth proceeds in all the cases. The computed microstructures for all the eutectic alloys of all of the binary systems belong to normal type of microstructure. The observed microstructure of eutectics and addition compounds are found different from those of pure components.

ACKNOWLEDGEMENT

Thanks are due to the Head Department of Chemistry, V K S University Ara 802301, India for providing research facilities.

REFERENCES

- [1]. R. del Sole, M. R. Lazzoi, G. Vasapollo, Synthesis of nicotinamide-based molecularly imprinted microspheres and in vitro controlled release studies, *Drug Deliv.*, 17(3), 130-137, (2010).
- [2]. S. R. Byrn, W. Xu, A. W. Newman, Chemical reactivity in solid-state pharmaceuticals: formulation implications, *Adv. Drug Del. Rev.*, 48, 115-136, (2001).
- [3]. J. F. Remenar, S. L. Morissette, M. L. Peterson, B. Moulton, J. M. MacPhee, H. R. Guzman, O. Almarsson, Crystal engineering of novel cocrystals of a thiazole drug with 1,4-dicarboxylic acids, *J. Am. Chem. Soc.*, 125, 8456-7, (2003).
- [4]. F. M. Murrey, A. Srinivasan, Nicotinamide inhibits HIV-1 in both acute and chronic in vitro infection. *Biochem. Biophys. Res. Commun.*, 210, 954-959, (1995).
- [5]. F. M. Murrey, Nicotinamide: An Oral Antimicrobial Agent with Activity against Both Mycobacterium tuberculosis and Human Immunodeficiency Virus, *Clinical Infectious Diseases*, 36, 453-460, (2003).
- [6]. N. M. Niren, Pharmacological doses of nicotinamide in the treatment of inflammatory skin conditions: a review *Cutis*, 77, 11-16, (2006).
- [7]. A. S. Girgis, H. M. Hosni, F. F. Barsoum, Novel synthesis of nicotinamide derivatives of cytotoxic properties. *Bioorganic & Medicinal Chemistry*, 14(13), 4466-4476, (2006).
- [8]. S. M. Haider, Synthesis of 7-Azaindole and Nicotinamide Derivatives Having Potential Therapeutic Activity. PhD thesis 1995. University of Karachi, Karachi.
- [9]. Abraham DJ, Mehanna AS, Wireko FC, Whitney J, Thomas RP, Orringer EP. Vanillin, a potential agent for the treatment of sickle cell anemia. *Blood*, 77(6):1334-41, 1991.
- [10]. S. B. Sonali, B. B. Sandip, N. B. Amrita, Interactions and incompatibility of pharmaceutical excipients with active pharmaceutical ingredients: a comprehensive review, *J. Excipients and Food Chem.*, 1(3), 3-26, (2010).
- [11]. B. L. Sharama, S. Tandon, S. Gupta, Characteristics of the binary faceted eutectic: benzoic acid –salicylic acid system, *Cryst. Res. Technol.*, 44(3), 258-268, (2009).
- [12]. H. Shekhar, Y. Roy, Thermodynamic interaction in alloys of Naphthalene-Imidazole system, *Nepier Ind. Adv. Res. Journal of Sci.*, 5, 113, (2010).
- [13]. U. S. Rai, H. Shekhar, Direct observation on solidification of binary organic alloys, *J. Thermal Analysis*, 39, 415, (1993).
- [14]. J. Sangster, Phase diagram and thermodynamic properties of binary systems of drugs, *J. Phy. Chem. Data*, 28, 889-931, (1999).

- [15]. K. P. Sharma, P. R. Shakya, R. N. Rai, Solid–Liquid Equilibria, Physicochemical and Microstructural Studies of Binary Organic Eutectic Alloys: Urea + 2-Aminobenzothiazole System, *Scientific World*, 10(10), 91-94, (2012).
- [16]. B.L Sharma, Structural models of faceted–faceted eutectic system vanillin–acenaphthene, *Materials Chemistry and Physics*, 78(3), 691-701, (2003).
- [17]. P. Gupta, T. Agrawal, S. S. Das, N. B. Singh, Phase equilibria and molecular interaction studies on (naphthols + vanillin) systems, *J. Chemical Thermodynamics*, 48, 291, (2012).
- [18]. Jürgen Gallus , Qiong Lin , Andreas Zumbühl , Sebastian D. Friess , Rudolf Hartmann, Erich C. Meister, *J. Chem. Educ.*, 78 (7), 961, (2001).
- [19]. G. F. V. Voort, “Binary Phase Diagrams and Microstructures,” *Materials Characterization*, Vol. 41, No. 2, 1998, pp. 69-79.
- [20]. H. Shekhar and Vishnu Kant, Some Studies on Pharmaceutical Eutectic: Nicotinamide - Benzamide System, *Int. J. Pharm. Tech. & Res.*, 4(4), 1486 (2012).
- [21]. K. Seefeldt, J. Miller, F. Alvarez-Nunez, N. Rodriguez-Hornedo, Crystallization Pathways and Kinetics of Carbamazepine- Nicotinamide Cocrystals From the Amorphous State by In Situ Thermomicroscopy, Spectroscopy and Calorimetry Studies, *J. Pharm. Sci.*, 96(5), 1147, (2007).
- [22]. J. D. Hunt, K. A. Jackson, Binary Eutectic Solidification. *Trans. Metall. Soc. AIME*, 236, 843, (1966).
- [23]. H. Shekhar, Vishnu Kant, Kinetic and Interfacial Studies on Transparent Organic Alloys, *J. Chem. Soc.*, 88, 947, (2011).
- [24]. H. Spengler, *Z. Metallk.*, 11, 384, (1957).
- [25]. V. V. Podolinsky, V. G. Drykin, Surface structure change of a crystal in solution *J. Crystal Growth*, 62, 32037, (1983).
-