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A PHARMACEUTICAL EUTECTICS: KEY ROLE IN DRUG DELIVERY

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ABSTRACT

Eutectics mixture, amongst other binary systems like cocrystals, solid dispersion, solid solution and inclusion complexes can be utilised to simultaneously enhance more than one characteristics of drugs like dissolution, permeability, stability etc. So far their utility is exploited to a large pace in metallurgy, however very little is achieved in the field of pharmaceuticals. References suggests that eutectics can be made very easily (sometimes spontaneously) both on laboratory scale as well as on industrial scale. The present review comprehensively and succinctly presents vital information like criteria of historical background formation, method of preparation and evaluation parameter of eutectics, which would help to exploit them in the pharmaceutical field.

KEYWORDS: Carrier, Eutectic mixtures, phase diagrams, crystal lattice.

INTRODUCTION

A eutectic system is a mixture of two or more components which melts at a single temperature which is generally lower than the melting point of the components presents in it.

Eutectic mixtures have several utilities for example they aid in refrigeration and washing of the snow in the frozen area. When sodium chloride is mixed in water, it leads to depression in the freezing point which aids in melting of snow, on one hand and formation of ice at a subzero temperature which helps in preservation of meat and storage of ice cream etc. Similarly eutectic mixture of ethylene glycol and water act as anti freeze in the vehicles, batteries and other energy storage devices used in polar regions. Lead tin alloy is used for soldering the electrical wires and in glass and ceramic industries.[1]

Now a day eutectics have gained some popularity in pharmaceutical field i.e. in the preparation of local anaesthetics of lidocaine and prolicaine, eutectic mixture is formed to enhance the transdermal penetration of lidocaine.[2]

The enhancement of dissolution in eutectics, by alteration of their thermodynamic functions like free energy can be explored to increase the aqueous solubility of poorly soluble drugs.[1] Sometimes solid dispersions of drugs show eutectic behaviour and leads to solubility improvement like in eutectic mixture of fenofibrate and polyethylene glycols.[3] Amongst the factors which favour the formation of eutectic mixtures between two compounds. A) compound that do not mix in solid state but mix readily on liquefaction. B) intimate physical interaction between eutectic forming compound to induce the depression in melting point. C) the tendency to form hydrogen bonding through weak van der waal's forces or dipole- dipole interactions which favour the formation of eutectic mixtures.[4] Because of possibility of formation of Eutectic mixtures between active pharmaceutical ingredients (APIs) and other inert substances which are often used as excipients, in the formulation.

History of eutectics in pharmacy literature

Eutectic mixtures were studied and classified under the category of solid dispersion and evenly related to the solid solution in literature of pharmaceuticals.[5] When one or more components are dispersed in a carrier or solid matrix, the system is defined as the solid dispersion.[6] However a eutectic and solid dispersion share the same features of phase separation (heterogenous structural organizations) in crystal lattice.[7] Because of these similar characteristics, eutectic mixture and solid dispersion of drugs were dealt together and these terms were used interchangeably.[8] For example, fenoglide being marketed as polyethylene glycol – fenofibrate is a solid dispersion and a eutectic mixture too, which is now termed as eutectic solid dispersion.[3] The first successful application of a eutectic mixture for topical anesthesia was credited discussed by Jules Aristide Bonain, the homogeneous mixture of cocaine hydrochloride, menthol and phenol was discovered by him, which can transform into homogeneous liquid at room temperature.[9] However, due to the toxic effects of cocaine and the caustic properties of phenol, this mixture was rarely used.

In the past, eutectics, for less stable amorphous drug formulations.[10] The first generation pharmaceutical solid dispersions (1960s), were prepared for improvement in bioavailability due to higher water solubility of the carrier. On the other hand it resulted into increase in the

stability owing to the change from amorphous to crystalline form and a corresponding decrease in solubility due to the same reason.[11]

Thus, in the subsequent generation solid dispersions (1970s to present) amorphous solid dispersion were prepared by using amorphous polymers to enhance the solubility and dissolution rates of the poorly soluble drugs. The literature on drug eutectics in early 1960s started with work and publication of Sekiguchi and Goldberg, they prepared the eutectic mixture of sulfathiazoles-urea and chloramphenicol-urea by using fusion method for enhancement in dissolution and bioavailability.[12] A well known eutectic of analgesic aspirin and 2-3 parts of glycerin or propylene glycols was prepared by mechanical mixing is used as ointment for topical application and this also enhance the shelf life by controlling its hydrolysis.[13] In current decades drug-drug eutectics have gained a lot of interest in context of multidrug therapy.[14] Eutectics have less popularity than solid dispersion and cocrystals but they appear to have potential to enhance stability and bioavailability of the poorly soluble drug.[15]

Pharmaceutical use of eutectic mixtures

Eutectic mixtures have a lot of applications in the pharmaceutical field. During preformulation stage compatibility studies is necessary step in the selection of excipients. Testing the eutectic mixture of drug and excipient helps in the prediction of probable physical incompatibility.[9] Eutectic mixtures are generally used in drug designing and delivery process.

Methods of preparations of eutectic mixtures

Eutectic mixtures are generally prepared by the following methods.

(1) Melting method (fusion method)

Melting method is also called as fusion method. This method was firstly employed by Sekiguchi and Obi who prepared physical mixture composed of sulfathiazole and urea. The process of formation of physical solution involved heating of components until they melt. The molten mixture settles rapidly while stirred continuously at low temperature of an ice bath. Supersaturation of mixture is achieved by sudden cooling on an ice bath. Due to these conditions substance molecules become “trapped” in a matrix of a rapidly solidifying system. The solid mass formed is then, pulverised and then sieved to standardize the size of grains obtained. This technique increases dispersion of crystals in the eutectic

mixture. Inspite of its widespread use fusion method has some limitations. It can be used only when the drug substance and the carrier mix homogeneously upon heating. Another important limitation of this method includes degradation of both the drug substance and the carrier at high temperature. Heating may cause evaporation of a volatile drug or a carrier. One approach to solve this problem is heating the mixture or melting under vacuum. Also, the process may be conducted under an inert gas, such as nitrogen, atmosphere which prevents the oxygen-initiated degradation of the drug or carrier. Another unfavourable condition of this method include a change in the mutual miscibility of the components during cooling, resulting in phase separation. Upon slow cooling of the mixture, appearance of the drug in a crystalline form was observed. On the other hand, rapid cooling promotes formation of amorphous solid dispersions.[20]

(2) Solvent method

Solvent method was first used by Tachbani and Nakamura who prepared the solid solution of liophilic β-carotene in a hydrophilic carrier– polyvinylpyrrolidone. In this method, physical mixture of a drug and a carrier is dissolved in a volatile solvent, i.e. chloroform or dichloromethane. Then, solvent was allowed to get completely evaporated at 23–65^{0}C, and the Solid dispersions dissolved solids form a layer of solid dispersion. The resulting film was dried and pulverized. The solvent used and its removal rate are very important factors, determining dissolution rate of drug substance in the solid dispersion thus obtained. They affect crystallographic structure of the resulting system. The main advantage of this solid dispersion preparation method is preventing degradation of the drug substance by maintenance of low temperature needed to vaporize the organic solvent. The disadvantages include high cost of production, difficulties with selection of an easily volatile solvent and its complete removal, possible side effects caused by solvent residues affecting chemical stability of the substance, as well as problem with reconstruction of the crystalline form.[6]

(3) Melt evaporation method

Solid dispersions are prepared also by dissolving drug in relevant solvent and the solution was incorporated with polyethylene glycol melted below 75^{0}C. The two solutions are mixed and the solvent is evaporated leaving the product layer which is dried until a fixed weight is achieved. The limitation of this method is the limited solubility of drug in solvents and their mixing with melted polyethylene glycol. Studies confirmed that 5 to 10% of liquid ingredients get incorporated into PEG 6000 without any significant loss of solid features. In

addition, liquid solvent used in this method is capable of forming polymorphic drug forms which then appear as precipitates in the resulting solid dispersion. One drawback of this method is the limited amount of drug introduced into solid dispersion that is only 10% of the whole system.[5]

(4) Melt extrusion method

Melt extrusion method for preparing solid dispersions was introduced recently. It is considered that this method is particularly useful to obtain dispersions of drug substances occurring in various polymorphic forms of different bioavailability. In the process of solid dispersion formation with the use of this technique drug substances have to be dissolved in polymer and remain in form of molecular dispersion even as the polymer solidifies. Melt extrusion method is a variation of the melting method. The process of melt extrusion can be divided into several stages, including: introduction of substrates into extruder, mixing and reduction of particle size, concentrating mass to be extruded into compact material of solid consistency, mass melting, homogenization and forcing the melt through extrusion tool.[21] Substance that play role of a carrier, e.g. polymer, is introduced into the feeder part of extruder through dosing hopper. By using appropriate technical solutions, the material can be easily transported inside a cylinder via a single or a double worm. Along the way it is premelt in the heat supplied from the outside source, produced by heating elements located on cylinder walls and by friction. Heating element has to be kept on constant temperature. The introduced substrates are mixed together, kneaded and subjected to melting. In the subsequent extruder part deaerating takes place, then, homogenization of the material and eventually, the intermediate reaches degassing zone. To ensure the uniform product thickness, the mass flow through the cylinder into the receiver part should be kept constant. The final stage of the process is grinding of the obtained extrudate for one minute using laboratory mill and sieving to separate particles larger than 355 μm. After extrusion completion the product is formed into tablets, granules or pellets Like in the traditional melting method, problem with use of the melt extrusion method may be mutual mixing of components and their sensitivity to temperature. However, due to the short-term sample exposure to high temperatures (about one minute), this technique may be employed to receive solid dispersions even for heat labile substances Extrusion method allows production of solid dispersions on a larger scale than a laboratory method.[22]

(5) Melt agglomeration method

This technique was used to create solid dispersions when a carrier acts also as a binding agent. In this case, solid dispersions may be prepared with simultaneous stirring of a heated carrier (binding agent), drug and excipients using a high-speed mixer above the melting point of the carrier. Also, solid dispersions may be prepared following addition of the dispersed drug together with the excipients to the already melted and heated carrier, or by adding of the molten carrier with the drug to preheated excipients Type of a binding agent, method of preparation and particle size, are parameters considered as critical in preparation of solid dispersion using this technique. Particle size determines solubility of the created system, mechanism of agglomerate formation and their size, distribution and concentration.[6]

(6) Grinding method

On laboratory scale this method is used for the preparation of eutectic mixtures. The function of grinding can be performed by using mortar pestle. On large scale vibratory mills, mechanical grinders are used. This method has some drawbacks, so this is not used conventionally.[23]

(7) Compaction method

In this method, sometimes unintentionally during the formation of tablets i.e. during wet granulations or during compression, the formation of eutectic mixture takes place. This may be due to intimate contact of components or due to rise in temperature during punching.[24]

Micro eutectic

The flow chart showing that when cohesive forces overcome the adhesive forces in the crystal lattice arrangement when one component is dispersed in another one then due to the isomorphous compound solid solutions are formed and due to non isoamorphous compound eutectic mixtures and solid dispersion are formed.[25] The second condition is that when adhesive forces are more than cohesive forces then formation of salts, inclusion complex and cocrystals are formed.[14] For example the lead–tin system, When tin (Sn, Z = 50, tetragonal) is added to lead (Pb, Z = 82, cubic), or vice versa.[26] Solid solution alloys is formed by them like copper–nickel system up to their solubility limits. As tin has smaller size leads higher solubility in lead (0–19%) whereas, the lead with larger size has lower solubility in tin (0–2.5%). This means up to 19% tin can be incorporated in the lattice structure of lead to form a homogeneous solid solution, which retains the lattice structure of lead because it is the major component (81%). When there is increase in the percentage of any one of the compound and

goes more than solubility, then there is a strain and disarrangement in the lattice of the solid solution. This strain and disarrangement is recovered by formation of aggregates and process of reorganisation into different phases which are together bounded and eutectic phase is constituted. The differentiation between solid solution and eutectic mixture is done in order that when different components are mixed in any ratio, they forms continuous solid solution but in eutectic mixture there is limited solubility in one another and discontinuous solid solution is formed. The discontinuous solid solution is called eutectic mixture. There are weak interphase bounderies for holding the solid solution domains, along with these boundaries atoms get dispersed and redistribute in solution of solid. The maximization of the strain is done by the deformity in the atomic arrangement and interphase bonding are also poor, this results into the increase in thermodynamic functions like free energy of eutectic phase.[3]

Law *et al.*, proposed a method for determination of the type of interaction b/w two components of a binary system using the pka value of both components.

However there is no mention of a range of pka value of these components which favour the formation of eutectic mixture.

The crystal structures of salts and cocrystal : when one component either a element or compound is incorporated in the lattice of another component and is bound by cohesive forces, it leads to the formation of variable stoichiometry by component or multicomponent, crystalline solid which is termed as a solid solution e.g. as in copper–nickel and symtriiodophenol– triiodoresorcinol solid solutions. Lattice structure of distinct substances (elements or components) or solid solution or their solid solution forms a eutectic mixture e.g. lead–tin, 1 and KNO_3–$NaNO_2$–$NaNO_3$ salt bath. The parent lattice structure of individual components can be retained in the eutectic mixture where the cohesive interaction between them overpower the adhesive interactions, however when the reverse happens it leads to the formation of distinct unique multicomponent crystal structures like cocrystals, salts etc.[21]

Micro structure of eutectic

The integrity of structures of solid solution and eutectics was better studied in inorganic systems. Inorganic alloys classification includes (i) solid solution alloys, and (ii) eutectic alloys. In ancient times eutectic mixtures and solid solutions were prepared by the fusion of

two or more solids in different ratios to give a product which has lower melting point than either of its components.[25]

A solid solution shows the range of melting or freezing point. Solidus is the temperature below which the material is in solid state, the temperature above which the material is in liquid state is known as liquidus. Solid and liquid phases exist simultaneously in between solidus and liquidus. On other point, eutectics have property that its melting point is lower than that of its components. It shows no range of melting point but it shows sharp peak of melting point this means that temperature of both solidus and liquidus are same. Solid solution is composed of two components i.e. one is solvent (major phase), another is solute (minor phase). Isoamorphous crystals generally forms solid solution while non isomorphous crystals forms eutectics.[1,26]

Drug and carrier selection criteria

The choice of drug and carrier based upon the two factors: one is selection of partner molecule by its design and another is prediction of its microstructure.[27]

The chemical groups like amide, amino acids, alcohol are responsible for the formation of eutectic mixture with different drugs. Hydrogen bonds play a crucial role in the formation of eutectic mixtures.[2]

The term “supramolecular synthon” was given by Desiraju and defined as the structural units in the superamolecules which are formed by intermolecular intractions which are known. The classification of synthon mainly depend on the type of functionl groups that take part in hydrogen bond to form superamolecular assembly. These are mainly classified as: Homosynthon (containing self complementary groups like carboxylic acid or carboxamide dimmers) or Hetrosynthon (containing the different functional groups like in acid pyridine or acid amide).[14]

Cambridge structure database (CSD) provide the facility for providing the supermolecular behaviour of a given functional group. In present CSD constitute about 2,50,000 crystal structure of organic compounds. By crystal structure of organic compound one can predict the formation of supermolecular synthon.[15]

The selection of carrier

As we know that properties of eutectic mixtures are generally affected by selection of drug and carrier. For API and carrier selection "hit and trial method" is used but it is time consuming and very costly. By using CSD, We can find out the pairs of conformers which can be best suited to drugs. When interaction between molecules takes place, then packing of the crystal takes place. CSD is used to study the interaction whether they are adhesive or cohesive. CSD software is very useful to study the type of intermolecular interaction and chances of formation of eutectic mixture depend.

By the use of CSD software, We can study the bonds, functional groups, atoms hydrogen bond acceptor, hydrogen bond donors etc.[21]

Partition coefficient

Partition coefficient also plays a major role in the prediction of eutectic composition of the compounds. In case if we use PEG carrier for preparing eutectic mixtures, we can calculate partition coefficient by using n-octanol or water. If the value of partition coefficient is high then it is considered that the interactions between drug and carrier are more favourable to form eutectic mixtures.[28]

Heat of fusion

Higher eutectic composition can be obtained when there is low heat of fusion of drug. Eutectic composition is determined by difference in melting point (crystal energy) between drug and carrier. Those compounds which exhibit a higher crystal energy show high eutectic composition by choosing carrier which show higher interaction with drug.[28]

Chemistry involved in Eutectics

Supermolecular chemistry is a useful tool for predicting chemistry involved in eutectic mixtures as there is manipulation in the assembly of crystalline solids. The interaction between molecules such as π- π stacking, engaged Van der Waal's forces, hydrogen bonding are in formation of eutectics. Supermolecular synthon are used for research in eutectics.[32] Cocrystals and eutectic system can be differentiated by illustrating the following example: benzoic acid combined with 4- fluorobenzoic acid which is structural analogus to it and forms solid solution, in second case benzoic acid combined with the penta fluoro benzoic acid to form cocrystal and with benzamide, it forms eutectic mixtures due to presence of amide-acid heterodimers, the benzoic acid –benzamide product is eutectic.[1]

In second example when curcumin is combined with dihydroxybenzene it forms cocrystal with cocrystal with 1,3- dihydroxybenzene and eutectic hydroquinine.

Density

In the eutectic mixture the component which had higher density is present in the vacant spaces of the second component whose density is lower. In this way the component of lower density accommodated the component with higher density, so the component with lower density is present in more proportions in comparison to the component with higher density. In simple words we could say that some new interactions had weakened the old bonds of both the components during eutectic mixture formation due to which melting point of both the components had decreased to a lower value.[33]

Structure of some drugs and carriers which form eutectic mixtures

Mechanisms for dissolution rate enhancement by eutectic mixtures

The mechanism of enhancement of dissolution rate by use of eutectic mixture is that when there is exposure of eutectic mixture to the gastrointestinal fluids then which is highly soluble get dissolved immediately and insoluble drug is left in a very fine subdivision state. For enhancing dissolution rate, a eutectic mixture with highly soluble conformer and poorly soluble drug is prepared. The poorly soluble drug get entrapped into interstitial space in molecule of. Due to this reason there is a faster release of the drug which is present in[34]. This is reported by Sekiguchi and co-workers.

Mechanism of stability enhancement

The preparation containing eutectic mixture has a enhanced shelf life as presence of eutectic mixture prevent hydrolysis of the formulation.[20] Being crystalline in nature, eutectic mixture shows high stability than other solid dispersion.[13]

Characterisation of the eutectic mixtures

Traditionally eutectic mixtures are characterise by the using phase diagrams but it is a tedious process and laborious too.

The prediction of formation of eutectics is a real challenging process as we all know formation of eutectic is only predicted by the melting point which is lesser than that of its individual constituents.[35] Phase diagrams are also prepared for prediction of eutectic mixture formation. The phase diagrams predicts the composition of compounds required for eutectic

formation.[31] spectroscopy and powder x-ray diffraction are commonly used for prediction of other solids which are multicomponents like salts and co crystals but eutectic mixtures are not properly characterize by these techniques as eutectic mixtures do not show change in spectroscopic and x ray diffraction pattern when compared to its individual components.[36] These show a slight difference in the spectrals peaks and x ray diffraction lines. The analysis by thermal method is best method for prediction of eutectics. SEM analysis is also done for the particle size determinations as described above that crystalline structure is formed by eutectic mixtures.

Differential scanning colorimetry (DSC)

DSC is the one and only technique which indicate about the eutectic phases. The higher entropy and weaker interactions in organisation of non random product are responsible for lower melting point of the eutectics. The physical mixture was heated in a DSC pan at a rate of heating 5^0C/min, then upon grinding, the formation of eutectic phases takes place. Like polymorphs, when temperature is increased breaking, reorganisation of bonds takes place that lead to formation of eutectic phases.[37] By DSC we can indicate that eutectic formation is enhanced by grinding. DSC thermograms shows a classical "v" shape in which molar ratio is represented at minimum point of "v" and this minimum point also represent temperature of eutectic point.[38]

Thermogravimetric analysis (TGA)

It is the technique of thermal analysis. In this technique change in mass (either loss or gain) is measured with respect to temperature or time in a controlled atmosphere. Generally this method is combined with other methods. TGA is of three types: (1) Dynamic TGA (in this case the sample is placed in environment of continues increase in temperature) (39) (2) Static TGA (When sample is maintained in the environment and change in temperature is denoted) (3) Quality TGA (When weight of the sample is kept constant during heating series).

The prediction of material composition is done by using TGA. Thermal stability of material is also predict by using this technique. TGA studied are the effective tool for the determination of oxidative stability of drugs, life time of drug product, product decomposition analysis, composition of material etc.[2,39,40]

Hot-stage microscopy (HSM)

Thermomicroscopy is another name of hot stage microscopy. In this technique microscopic method and thermal analysis are used together for studying the physical and chemical properties of the material with respect to functions of temperature and time. In this technique observations are done during the heating and cooling of few quantity of substance on a microscopic slide. In this techniques crystallized samples are used. Polymorphs and solvates are characterized.[35,41]

Powder x ray diffraction

For characterization and identification of crystalline material powder x ray diffraction technique is mostly used. On the basis of wavelength of incident rays and angle(ɵ) where constructive interferences takes place, the unknown material can be identified.[7,16] Spacing between crystal lattice atoms which can produce constructive interferences can be determined by using Bragg's equation. In crystal structures there are many plane of atoms, then the reflection from all plane are used to determine the crystal structure.

In case of eutectic mixtures PXRD result of eutectic shows the similar pattern as that of pure component. There is only slightly difference in the x ray diffraction lines.[41,42]

Spectroscopic characterization

FTIR spectroscopy

The prediction of intermolecular interactions and study of compatibility between drug and conformer are done by using FTIR spectroscopy. The chemical conformation of compound can be described by this technique. A very small amount of sample is required for analysis (just 10^{-7}- 10^{-8} g in case of solid) this technique is fast and gives 2d –IR spectra which resemble to NMR correlation spectroscopy. This 2D NMR firstly applicable to solutions but now a day it can be used for larger molecules the information of molecular structure and dynamics is given by 2D IR spectra.[43] Aakeroy et. *al*. reported that on the basis of involvement of carboxylic acid in hydrogen bonding, eutectics can be differentiated from the salts. IR spectroscopy give response with respect to changes in vibrational modes of covalent bonds due to changes in intermolecular. In case of eutectics there is slightly change in the pattern of spectral line in comparison to the individual ccompounds.[36,40,44]

Raman spectroscopy

Most of APIs are more polarisable and they produce strong raman bands as compared to the excipients. The IR spectrum generally cover a low frequency range (about several tens of cm^{-1}) to about $4000cm^{-1}$. The study of drug crystallinity is done in the low frequency region. Interpretation is same as that of tetraherz spectroscopy. Raman bands which are produced by amorphous substances are broad and below $400cm^{-1}$ and shows tendency to disappear (43). Glass and plastics packaging are used for pharmaceutical formulations and the analysis is non destructive but due to the long exposure to the UV light some samples may get deteriorated. The amount of sample is depend upon the type of setup use, the setup may be micro, mini or nano. For micro not more than several milligrams of solids and in case of nano, a nanosize spot is suitable. In pharmaceuticals, raman spectroscopy is applicable for investigation of single crystals, powders or lump of substances. Transmission raman spectioscopy is reliable to analyse polymorphic content in bulk samples. Two types of instruments are used for raman measurements one is dispersive spectrometer and another is fourier transform spectrometer. The dispersive spectrometer involves a visible region, gratings and detectors (silicon charged coupled devices). The FT R is operated with NIR laser, an interferometer and a semi conductor detector. Strong signals are given by the dispersive spectrometer and minor component can be detected by this device while FT R gives weaker signals, and these are only applicable to quantitative analysis. In case of eutectics there is slightly change in the pattern of spectral line in comparison to the individual compounds. For example IR raman analysis shows curcumin eutectic vibrational frequencies which are similar to the individual compounds i.e. for curcumin phenolic OH stretch at $3510.9cm^{-1}$ was shifted to 3508.7 cm^{-1}. There is slightly change in spectral lines.[2,16]

Teraherz spectroscopy

In THz spectroscopic region of molecular solids composed of bands which arise from the vibrations which are intermolecular such as (hydrogen bonds, vander Waals interactions).

The spectrum arise from Teraherz Spectroscopy is only depend on the temperature. They show sensitivity towards humidity and hydration of material. In this technique crystalline shows sharp band but in case of amorphous, the bands are broad and in certain case there is absence of bands. For differentiating and characterization of enantiomers, this technique is used. THz radiation can easily penetrate through pharmaceutical tablets. Pharmaceutical Tetraherz time domain spectroscopy is used.[45] Femtosecond laser is used to produce Thz

pulses in which beam get splitted into two parts, one is excitation beam another one is reference beam. The reference beam gets penetrated through the sample and time is denoted for radiation coming out through the sample. Signal can be measured a function of time delay between sample and reference beam.[27]

CONFLICT OF INTEREST

There is no conflict of interest.

CONCLUSION

Although eutectic mixture can proved to be of great benefit in the pharmaceutical formulation, till date very little is done in this direction. The studies include predictions of possibilities of benefits of eutectics. However the work related to formulation and evaluation of these binary system is still in pioneer stage. The future prospectives of eutectics in pharmacy are bright. Hopefully the coming era will witness more concrete results to fulfill the objective of marketing of eutectic drugs and carriers conjugates for benefit of humanity.

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