

Physical Characterization of Pharmaceutical Solids

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Solubility of Pharmaceutical Solids

David J. W. Grant*University of Minnesota, Minneapolis, Minnesota***Harry G. Brittain***Ohmeda, Inc., Murray Hill, New Jersey*

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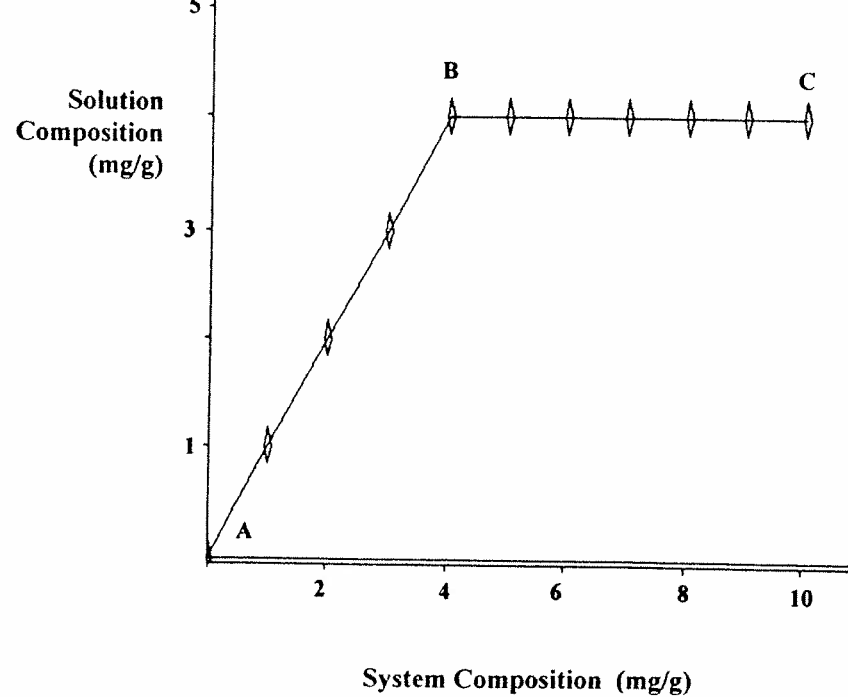


Fig. 5 Phase solubility plot for a pure solute.

When an impurity is present in the solute, the system is unlikely to be saturated with the additional component, and an additional contribution to the overall solubility will result. Application of the phase rule equation indicates that a plot of system composition versus solution composition now consists of three linear segments. When the solvent is not saturated with respect to either the analyte or its impurity, the number of degrees of freedom equals two, indicating that the concentration of each species varies linearly with the amount of solid added. This is illustrated by line segment D-E in Fig. 6. Owing to its large percentage in the solid, the analyte species will first saturate the solvent, and one solid phase will result. This effect decreases the number of degrees of freedom to one, which corresponds solely to the concentration of the impurity. At this point (segment E-F in Fig. 6), there can be no change in the concentration of the analyte as the amount of solid is increased. Finally, if enough solid is

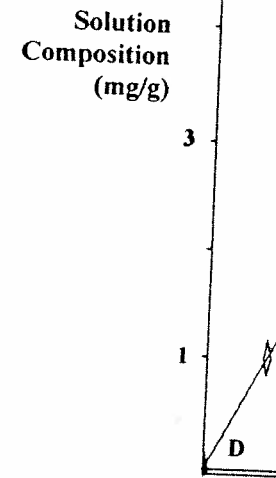


Fig. 6 Phase solubility plot for a substance and 25% of an impurity.

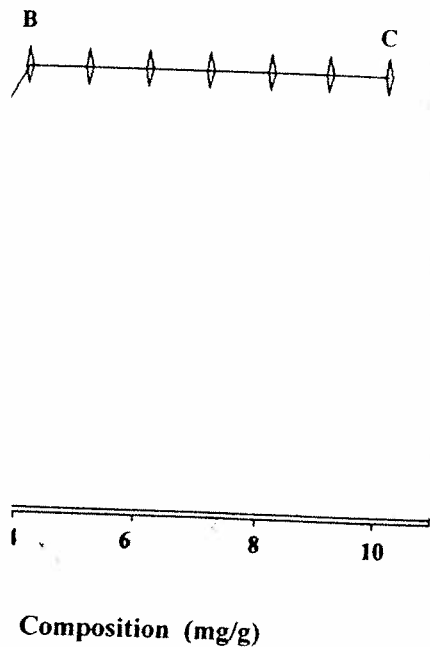
added, the system becomes saturated with respect to both components, and the number of degrees of freedom becomes zero, resulting in a plateau in solution composition.

When the solubility of the analyte is reached, the impurity species will calculate the weight purity by computing the slope of the line segment D-E.

$$\% \text{ purity} = (1 - \text{slope}) \times 100$$

The presence of more than one solid phase will result in a plot of system composition versus solution composition consisting of three linear segments.

During the analysis of a sample, the concentration of the impurity species is rarely reached. F



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e solute, the system is unlikely to be and an additional contribution to the of the phase rule equation indicates that ion composition now consists of three it saturated with respect to either the rees of freedom equals two, indicating ries linearly with the amount of solid it D-E in Fig. 6. Owing to its large es will first saturate the solvent, and decreases the number of degrees of to the concentration of the impurity. can be no change in the concentration ncreased. Finally, if enough solid is

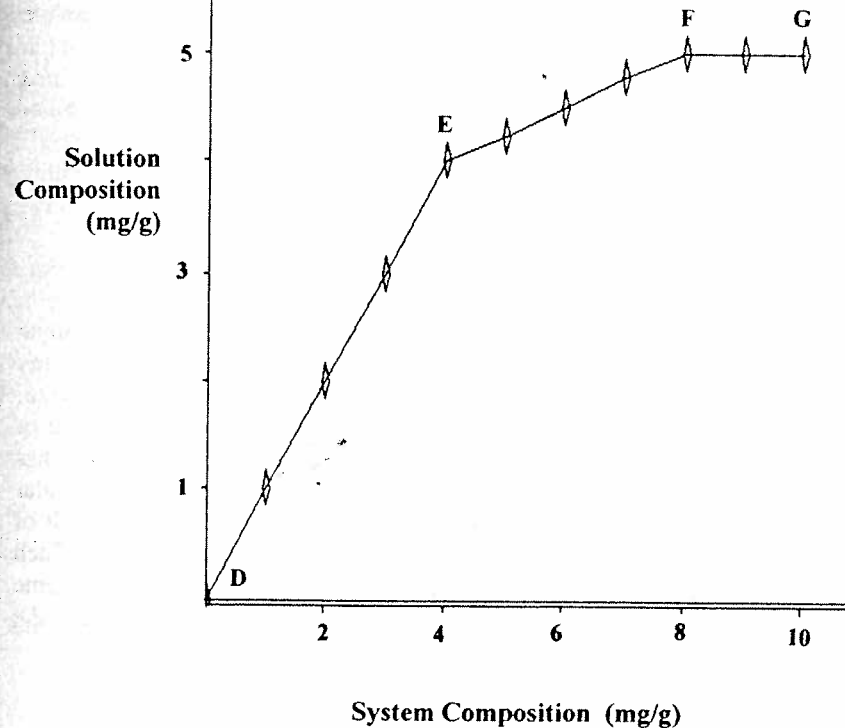


Fig. 6 Phase solubility plot for an impure solute consisting of 75% of the analyte substance and 25% of an impurity.

added, the system becomes saturated with respect to the impurity, and the number of degrees of freedom becomes zero. At this point (segment F-G in Fig. 6), a plateau in solution composition is reached, and no additional solid can be dissolved in the solvent.

When the solubility data are plotted as in Figs. 5 and 6, it is easy to calculate the weight purity of the analyte sample. This information is obtained by computing the slope of segment E-F and using the relation

$$\% \text{ purity} = (1 - \text{slope}_{EF}) \times 100 \quad (10)$$

The presence of more than one impurity in a material will yield additional segments in the plot of system composition versus solution composition.

During the analysis of real samples, the saturation limit of any impurity species is rarely reached. For that reason, the phase solubility curves normally

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