On the basis of solubility, dissolution, and kinetic parameters probable mechanism shall be proposed.

**Scheme-1**

Piszkiewicz model was used to explain the effect of this research work [1, 2], which is best suited for the experiment results of chapter –IV and V. The catalytic effect of SLS micelles reveals that the site of reaction is probably the interfacial region of Gouy – Chapmen and stern layers.

Few report have been appeared which reveal the occurrence of some reaction at the junctional region of the Gouy – Chapmen and stern layers.

According to Piszkiewicz the number of detergent molecules aggregate to form catalytic micelles.

\[ nD + S \rightleftharpoons DnS \quad .......... \ (1) \]

Where, \( nD = \) No. of Detergent molecules

\( S = \) Drug  [Duxletine hydrochloride, Domperidone]

The micelles form an adduct with drug and solubilize in inner core.

\[ nD + \text{Drug} \rightleftharpoons \text{Drug} \ldots Dn \ (\text{adduct}) \quad .......... \ (2) \]

Now in aqueous medium \( H_2O \) molecule react as nucleophile.

\[ \text{Drug} + \ldots Dn + H_2O \rightleftharpoons [H_2O \ldots \ldots \ldots \text{Drug} \ldots Dn] \quad .......... \ (3) \]

\[ \text{Fast} \quad \text{(Intermediate)} \]

\[ \text{Drug} + Dn + H_2O^+ \quad .......... \ (4) \]

In fast step the drug release and the structure of micelles as well as drug remains unchanged.
Scheme-2

This model assume that the rate of release of drug is first order with respect to the amount of encapsulated drug, one hypothesis of drug mechanism suggests that drug release does not destroy micelles, so that their number is kept constant. The amount released is proportional to that amount of drug remaining in the micelles.

This model assumes that number of micelles remain constant and the following mechanism is proposed.

Where DS = Diclofenac Sodium
There are a number of possible loci of solubilization for a drug in a micelle, as represented in Figure 7.1.

Accordingly, hydrophilic drugs can be adsorbed on the surface of the micelle, drugs with intermediate solubility should be located in intermediate positions within the micelle such as between the hydrophilic head groups of PEG. Micelles in the palisade layer between the hydrophilic groups and the first few carbon atoms of the hydrophobic group, that is the outer core and completely insoluble hydrophobic drugs may be located in the inner core of the micelle. The existence of different sites of solubilization in the micelle results from the fact that the physical properties, such as microviscosity, polarity and hydration degree, are not uniform along the micelle.
Scheme-4

The ionic strength can influence significantly the solubilization of a drug in micellar solutions, especially in case of ionic surfactants. The addition of small amounts of salts decreases the repulsion between the similarly charged ionic surfactant head groups, thereby decreasing the CMC and increasing the aggregation number and volume of the micelles. The increase in aggregation number favors the solubilization of hydrophobic drugs in the inner core of the micelle. On the other hand, the decrease in mutual repulsion of the ionic head groups causes closer packing of the ionic surfactant molecules in the palisade layer decreasing the volume available for solubilization of polar drugs. The addition of salts to solutions of PEG nonionic surfactants may also increase the extent of solubilization of hydrophobic drugs because of the increase in aggregation number (Fig.7.2).

![Image](image-url)

**Fig.7.2: Mechanism for Scheme 4**

The above schemes are consistent with experimental findings.
References:
