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Review Article

SCIENTIFIC BASIS FOR USING MEDICATED GHRITA IN AYURVEDIC SYSTEM OF MEDICINE

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Abstract

Ayurveda is the Ancient Indian medical science based on herbal remedies. In Ayurvedic system of medicine some of the drugs are administered as fat soluble preparation. This is unique concept of Ayurveda to administered drug in fat soluble form. In the present scientific world every concept has to be validated scientifically for its global acceptance. This article aims to provide probable scientific explanations for using medicated ghrita (ghee) in Ayurvedic system of medicine and its clinical importance. Drug absorption is determined by many important factors among which solubility of the drug is the major determinant. Regardless of the route of administration, drugs must be in solution to be absorbed. Unless given intravenously, a drug must cross several semi-permeable cell membranes before it reaches the systemic circulation. Cell membranes are biologic barriers that selectively inhibit passage of drug molecules. The membranes are composed primarily of a bimolecular lipid matrix, which determines membrane permeability characteristics. Therefore drug in lipid soluble form is more permeable than water soluble form. There are many more explanations in the favor of this concept which will be discussed in this article that helps reader to conclude that drug in fat soluble form are more permeable than water soluble drug.

Key words: Ayurveda; Ghee preparation; Lipid soluble drugs; Solubility.

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INTRODUCTION

In Ayurvedic system of medicine mostly the drugs are given as medicated Ghrita (ghee). There are approximately 650 Ghrita preparations described in Caraka Samhita and similarly in other Ayurvedic texts. Therefore a curiosity arises why so many Ghrita preparations are described in Ayurveda, is there any logic behind using the drug in Ghrita form (fat based)? There are many factors that influence the bioavailability of the drug in human beings. An overview of the patient specific and drug specific variables that can affect drug absorption following oral administration of drugs are: Drug solubility, permeability and rate of in vivo dissolution.[1]

Product bioavailability can also be markedly influenced by patients attribute such as:[2]

- Physiological status
- Site of drug absorption
- Membrane transport
- Presystemic drug metabolism{intrinsic variable}
- Extrinsic variables such as effect of food or concomitant medication.

Physiochemical Determinants of Passive Membrane Permeability

Role of Solute Hydrogen Bonding Potential and Volume- Hydrogen bond potential and volume of solutes contributes to permeability and suggest that the nature of permeability limiting micro-environment within the cells depends on the properties of specific solutes. Permeability depends upon solute structural properties. The question that how drug passes from Gastrointestinal tract to blood stream is a complex question. The extent of absorption has generally been appraised indirectly by the speed of onset of degree of pharmacological action or by the rate of appearance of drug in plasma or urine; these criteria of absorption are complicated by the variables of drug distribution, metabolism and excretion. There is wide spread recognition that the ingestion of a meal is associated with a number of physiological changes (gastric pH, gastric emptying, hepatic blood flow, etc.) that can significantly alter the rate and extent of drug absorption. It is also well recognized that the components of food can alter drug absorption through alteration in drug solubility. The nutritional status of a patient can also contribute to variability in the pharmacokinetic of certain drug. The more recent findings that grape fruit juice can increase bioavailability of certain drugs by reducing presystemic intestinal metabolism has lead to renewed interest in the area of Food- Drug interactions. Drug absorption is determined by the drug's physiochemical properties, formulations, and route of administration. Dosage forms (eg. tablets, respules, capsules, solution etc.) consisting of the drug and other ingredients are formulated to be given by various routes. Regardless of the route of administration, drug must be in solution to be absorbed. Unless given through IV (Intra venous) a drug must cross several semi permeable cell membranes before it reaches the systemic circulation. Cell membranes are biological barrier that selectively inhibit passage of drug molecules. The membrane is composed of a bimolecular lipid matrix which determines membrane permeability characteristics. Drugs may cross cell membrane by Passive diffusion, Active transport, or Pinocytosis.[3]

Passive diffusion

Drug diffuses across a cell membrane from a region of high concentration to one of low concentration. Diffusion rate is directly proportional to the gradient but also depends on the molecule lipid solubility, size, degree of ionization and the area of absorptive surface. Because the cell membrane is lipid, lipid soluble drug diffuse most rapidly. Small molecules tend to penetrate more rapidly than larger ones.[4]

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However whether a drug is acidic or base most absorption occur in small intestine because surface area is larger and membrane are more permeable.Most drugs are weak organic acids or bases, existing in un-ionized and ionized forms in an aqueous environment. The un-ionized form is usually lipid soluble (lipophilic) and diffuses readily across cell membranes. The ionized form has low lipid solubility (but high water solubility—i.e. hydrophilic) and high electrical resistance and thus cannot penetrate cell membranes easily. The proportion of the un-ionized form present (and thus the drug's ability to cross a membrane) is determined by the environmental pH and the drug's pK_a (acid dissociation constant). The pK_a is the pH at which concentrations of ionized and un-ionized forms are equal. When the pH is lower than the pK_a, the un-ionized form of a weak acid predominates, but the ionized form of a weak base predominates. Thus, in plasma (pH 7.4), the ratio of un-ionized to ionized forms for a weak acid (eg, with a pK_a of 4.4) is 1:1000; in gastric fluid (pH 1.4), the ratio is reversed (1000:1). Therefore, when a weak acid is given orally, most of the drug in the stomach is un-ionized, favouring diffusion through the gastric mucosa. For a weak base with a pK_a of 4.4, the outcome is reversed; most of the drug in the stomach is ionized. Theoretically, weak acidic drugs (eg. aspirin) are more readily absorbed from an acid medium (stomach) than are weakly basic drugs (eg, quinidine). However, whether a drug is acidic or basic, most absorption occurs in the small intestine because the surface area is larger and membranes are more permeable.[5][6]

Facilitated Passive Diffusion

A carrier molecule in the membrane combines reversibility with the substrate molecule outside the cell membrane and the carrier substrate complex diffuse rapidly across the membrane releasing the substrate at the interior surface.

Dissolution

The rate of dissolution is a key target for controlling the duration of a drug's effect, and as such, several dosage forms that contain the same active ingredient may be available, differing only in the rate of dissolution. If a drug is supplied in a form that is not readily dissolved, the drug may be released more gradually over time with a longer duration of action. Having a longer duration of action may improve compliance since the medication will not have to be taken as often. Additionally, slow-release dosage forms may maintain concentrations within an acceptable therapeutic range over a long period of time, as opposed is quick-release dosage forms which may result in sharper peaks and troughs in serum concentrations.[7][8]

The rate of dissolution is described by the Noyes–Whitney equation as shown below:

$$\frac{dW}{dt} = \frac{DA(C_s - C)}{L}$$

Where,

- $\frac{dW}{dt}$ is the rate of dissolution.
- A is the surface area of the solid.
- C is the concentration of the solid in the bulk dissolution medium.
- C_s is the concentration of the solid in the diffusion layer surrounding the solid.
- D is the diffusion coefficient.
- L is the diffusion layer thickness.

As can be inferred by the Noyes-Whitney equation, the rate of dissolution may be modified primarily by altering the surface area of the solid. The surface area may be adjusted by altering the particle size (e.g. micronization). For many drugs, reducing the particle size leads to a reduction in the dose that is required to achieve the same therapeutic effect. However, it should be noted that although the reduction of particle size

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increases the specific surface area and the dissolution rate, it does not affect solubility.[9][10]

The rate of dissolution may also be altered by choosing a suitable polymorph of a compound. Different polymorphs exhibit different solubility and dissolution rate characteristics. Specifically, crystalline forms dissolve slower than amorphous forms, since crystalline forms require more energy to leave lattice during dissolution. The most stable crystalline polymorph has the lowest dissolution rate. Dissolution is also different for anhydrous and hydrous forms of a drug. Anhydrous often dissolve faster than hydrated; however, anhydrous forms sometimes exhibit lower solubility.

Chemical modification by esterification is also used to control solubility. For example, searate and estolate esters of a drug have decreased solubility in gastric fluid. Later, esterases in the GIT wall and blood hydrolyze these esters to release the parent drug.

Blood brain barrier by simple diffusion

Substance with high lipid solubility may move across the blood- brain barrier by simple diffusion. The rate of entry of compounds that diffuse into the brain depends on their lipid solubility, as estimated by oil/water partition coefficients. For example, the permeability of very lipid-soluble compounds, such as ethanol, nicotine, iodoantipyrine and diazepam, is so high that they are extracted completely from the blood during a single passage through the brain. Hence, their uptake by the brain is limited only by blood flow.

DISCUSSION

Drug action depends upon its solubility and absorption. Media of drug administration and route of drug administration both have equal importance in determining the drug absorption rate. Passive diffusion facilitates fast absorption of fat soluble drug further potentiated by more dissolution of drug in lipid. Esterification of drug helps in microinonization and converting the crystalline form of drug in amorphous form that augment the absorption of drug. Chemical esterification is also helpful in controlling solubility and proper site of drug absorption. In Ayurvedic science of medicine a lot of medicated oil is prescribed for various diseases even in Heart diseases and liver diseases probably the reason behind that the fast absorption of drug at targeted site.

CONCLUSION

Thus from above discussion it is very clear that absorption of fat soluble drugs are much more than water soluble drugs, moreover bioavailability of fat soluble drug is also higher than water soluble drug. There are many contributory factors in enhancing the drug absorption like lipid nature of cell membrane that facilitates passive diffusion of lipid soluble drugs, non-ionized nature of fat soluble drugs that helps in attaining highest concentration of drug inside cell, highest dissolution rate of fat soluble drugs, esterification of drugs etc.

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