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Hydrophobicity, Transport and Target Sites of Action Are Important for the Activity of Many Drugs

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Abstract

The Hydrophobicity mean the compounds which insoluble in water i.e., hate the water (not love the water). May be these compounds are lipid soluble, but not actually. This means these compounds may across the cell membrane of the cell. This transport of compounds through, simple diffusion, passive transport (active transport), transport by carrier (amino acids carrier), pinocytosis. And the binding of drugs with tissue (may be receptors or tissue reservoir as (fatty tissue and lipid soluble vitamins) and the carbohydrates (glucose convert to glycogen in the liver).

Keywords: hydrophobicity, transport of drug, tissue binding drug, lipid solubility, Blood Brain Barrier (BBB)

1. Introduction

Where the animal and human cell the major content of cell membrane is lipid content, so when we want to enter the drug to the cell or organ must be we take in consideration the drug soluble in lipids or at least not love of the water (hydrophobicity). This concept it is the major when we design new drug, but may be present exception for example the levo Dopa is more polar than Dopamine but levo Dopa across the blood brain barrier while the dopamine not across, this cross of levo Dopa via the amino acid carrier which transfer it to the brain not due to the lipid solubility of it. Also the A, D, E, K are highly lipid soluble across the major concept of hydrophobicity across the blood brain barrier, hence the A, D ,E, K vitamins migrate from blood circulation to the fatty tissue before reach to the blood brain barrier mainly. So in spite the importance of hydrophobicity, but there are other factors share in the activity other than hydrophobicity e.g., the transport of drugs to the cell of the organ which is target for the drug, the transport may be according to the know mechanisms of transportation e.g., passive diffusion according to concentration of drug which transport from the high concentration of out cell or organ to the in cell or organ, active transport which the transfer of drug and need to

energy to enter the cell or the organ, some compounds need to carrier to enter the cell or organ for e.g., the amino acids carrier which transport the amino acid from blood circulation to the target organ and lastly some of materials transfer by pinocytosis mechanism where the organ or cell engulf the material wanted (amoeba), as well as previous mentioned if the drug reach to its receptor will be give the action, hence not necessary to across blood brain barrier.

Note. That if the hydrophobicity constant more than 2 will be across the BBB if present its receptor in the blood.

N.B. the acetyl salicylic acid in dose 75mg, 81mg and 100mg used as helper factor to dissolve the brain clot, however the acetyl salicylic acid not cross BBB, but act as antiplatelet aggregations in the general circulation before BBB, also the narcotic drugs have hydrophobicity constant more than 2 and cross the BBB and give the central effect due to the transportation to the brain which have the narcotic receptors.

2. Chemistry and Discussion

Table 1. Hydrophobicity constant (π value)

Fragments	**π value**
Phenyl moiety	2
C not aromatic	0.5
CL	0.5
Nitrate ester (O-NO2)	0.2
Intramolecular hydrogen bond (IMHB)	0.65
S	0.00
Carboxylic group (0=CO)	-0.7
Amide, Imide (O=CN), (CN=)	-0.7
OH(Phenolic)	-1
Ether	-1
Amine	-1
Nitro aliphatic	-0.85
Nitro aromatic	-0.25

N.B. The hydrophobicity constant equal to Logharism of partition coefficient (LogP value). If the logP Value less than 0.5 the compound is water soluble, if the logP value more than 0.5 the compound is water in soluble and if the logP value equal 2 the compound is able to cross BBB, as examples:

1) Dopamine and Levo Dopa

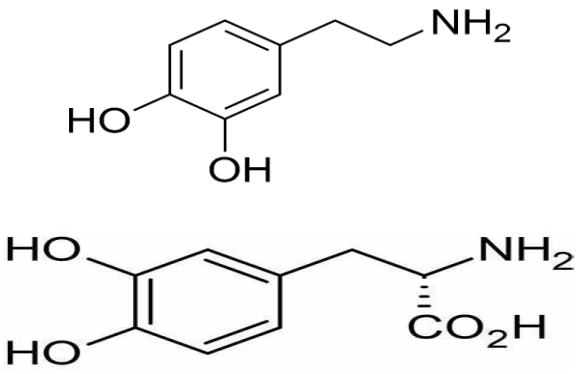

Figure 1.

Calculation of the Hydrophobicity π value (LogP value)

Dopamine	Levodopa
2OH = -2	2OH = -2
NH2 = -1	NH2 = -1
2 Aliphatic carbon = 1	COOH = -0.7
Phenyl ring = 2	Phenyl ring = 2
	2 Aliphatic carbon = 1

LogP of Dopamine = 0, While LogP of Levodopa = -0.7.

So the levodopa cross BBB, not due to hydrophobicity constant, but due to amino acid carrier transportation.

2) Anileridine narcotic analgesic

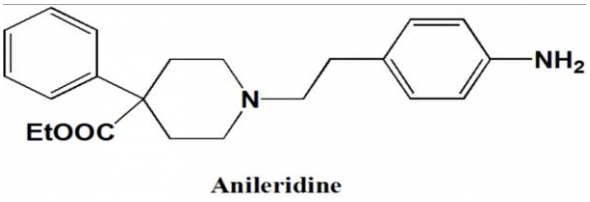

Figure 2.

Calculation of the Hydrophobicity π value (LogP value)

2 amines = -2,

8 aliphatic carbon = 4

2 phenyl rings = 4

1 ester = -0.7

LogP value = 5.3 (cross blood brain barrier)

3) Ibubrufen (NSAID) analgesic

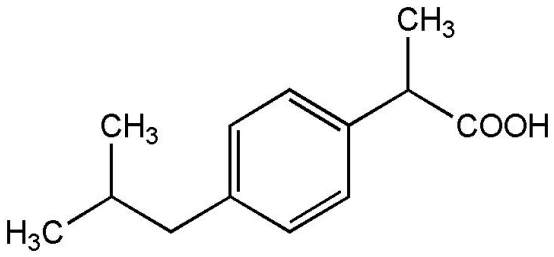

Figure 3.

Calculation of the Hydrophobicity π value (LogP value)

1 phenyl ring = 2

6 aliphatic carbon = 3

COOH = -0.7

LogP value = 4.3 (cross the blood brain barrier)

4) Diethylstilbesterol (DES)

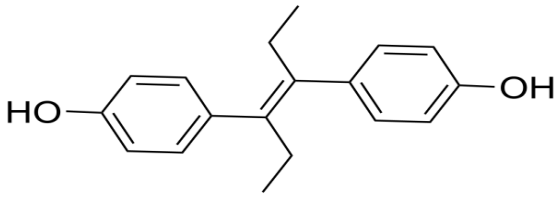

Figure 4.

Calculation of the Hydrophobicity π value (LogP value)

6 aliphatic carbon = 3

2 phenyl rings = 4

2 OH = -2

LogP value = 5 (cross blood brain barrier), but act on its receptor out the brain.

The lipid soluble vitamins A,D,E,K.

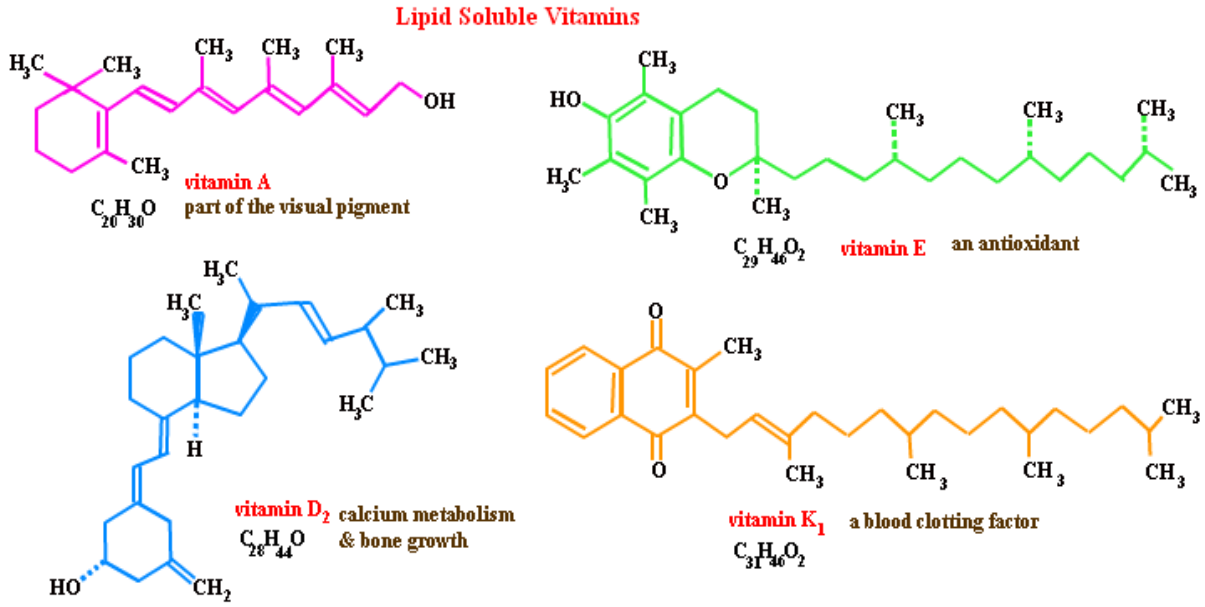

Figure 5.

From the previous structures we note the hydrophobicity more than 2, but these vitamins play its role in the body and the excess depot in adipose tissue not cross the BBB.

Drugs have hydrophobicity constant π value more than 2 but not cross BBB due to its receptor out of brain as Bisoprolol.

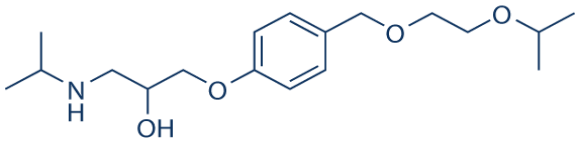

Figure 6.

Calculation of the Hydrophobicity π value (LogP value)

3 ether linkage = -3

OH = -1

Amine = -1

Phenyl ring = 2

12 aliphatic carbon = 6

LogP value = 4

Also not cross BBB due to it act on B1 receptor on heart.

3. Conclusion

The Hydrophobicity constant (π value) is significant in pharmacological action of many drugs, where the value is more than 2 may be cross the blood brain barrier if act in the brain or to penetrate the cell membrane to act on the cell of the organ and lastly may be stored in adipose tissue e.g., Lipid soluble vitamins and anti psychotic drug e.g., fluphenazine decanoate which used as long acting anti psychotic drug where stored in fatty tissue and release across the month.

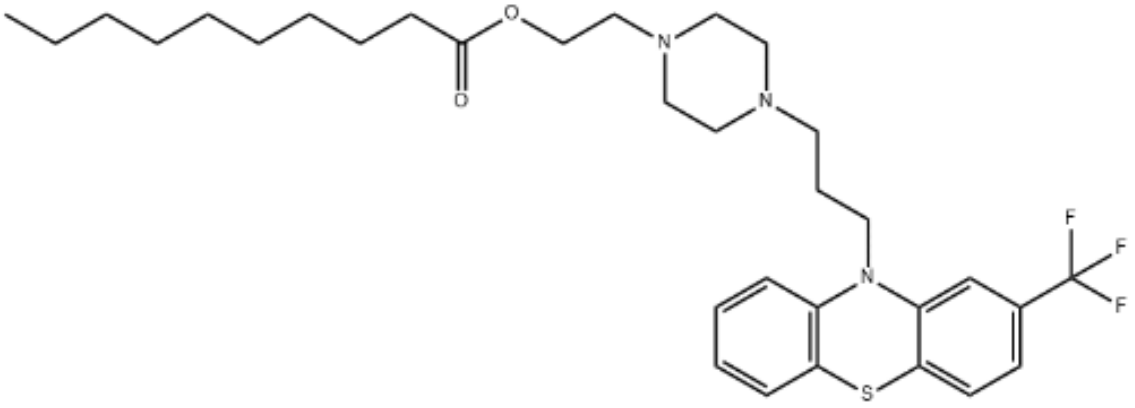

Figure 7.

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