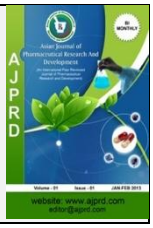
Available online on 15.12.2022 at http://ajprd.com

Asian Journal of Pharmaceutical Research and Development

Open Access to Pharmaceutical and Medical Research

© 2013-20, publisher and licensee AJPRD, This is an Open Access article which permits unrestricted non-commercial use, provided the original work is properly cited



Open Access

Review Article

Pharmacological Vunerability of Chemophoric Groups

Luv Kush

Sardar Bhagwan Singh University, Balawala, Dehradun-248001 Uttarakhand, INDIA

ABSTRACT

Abstract:

The drugs target the pathological proteins for the pharmacological intervention through their vunerability of chemophoric and congate groups [1-3] at therapeutic level. They are essential for binding affinity, intrinsic efficacy and bioavailability. They are introduced in bioactive molecules by replacement of hydrogen atoms. They are implicated in SAR modifications and interactional participation with receptor or enzyme or target protein. The pharmacological influence of them is delineated here.

Keywords: Hydrogen atom, Chemophoric, pharmacological, Vunerability, Congate group.

ARTICLE INFO: Received 05 Sept. 2022; Review Complete 28 Oct. 2022; Accepted 20 Nov. 2022; Available online 15 Dec. 2022

Cite this article as:

Kush L, Pharmacological Vunerability of Chemophoric Groups, Asian Journal of Pharmaceutical Research and Development. 2022; 10(6):134-136.

DOI: http://dx.doi.org/10.22270/ajprd.v10i6.1194

*Address for Correspondence:
Luv Kush, Sardar Bhagwan Singh University, Balawala, Dehradun-248001 Uttarakhand, INDIA

INTRODUCTION

Hydrogen atom is an indispensable chemical entity of organic medicinal compounds. The replacement of hydrogen by diverse chemophoric group cause perturbation. They are pharmacological vunerable for influencing lipophilic efficiency, electron density, steric environment, bioavailability, SAR and ligand's interaction with target protein. The pharmacological vunerability specify desired bioaction by chemopharmacophoric groups [4-7]. The majority of drugs have hydrophobic groups for the lipophilic efficiency, optimal absorption and oral bioavailability. The practice of medicinal chemistry classifies chemophoric groups as saturated and unsaturated, hydrophobic and hydrophilic, isoteric and biososteric, haptophoric and pharmacophoric, acidic and basic groups (highly ionized at physiological pH).

Theoretical Methodology:

The chemophoric acidic and basic group's are related to pka and their unionized and ionized concenterations which are calculated by Henderson-Hasselbalch equation. The unionized molecules cross biomembrane for the effective absorption. The carboxylic, enolic and phenolic are acidic in nature. The carboxylic is prototype group which is bioisosteric to sulfenic, phosphonic, tetrazole and 3-hydroxy isoxazole. They are useful in SAR modifications and salt formation. There is strong ionic interaction with basic aminoacids-Lysine present in enzyme and receptor protein. The acidic character imparts pharmacological vunerability to anti-inflammatory drugs, beta-lactam, antibiotics, barbiturates and antiseptics.

The basic chemophoric groups are amines, amidines, guanidines and nitrogen heterocyclics. They are highly polar and ionized bases, form quaternary ammonium salts. The high pka's limits CNS entry. The aspartic and glutamic acids of receptor proteins have carboxylates interactions.

The primary aliphatic amines have less specific effects than secondary and tertiary amines. The acylation deactivates the amines. Diamines and polyamines are more active than monoamines and aromatic amines are more toxic than aliphati amines.

The chemophoric hydrophobicity is attributed to methyl and aryl groups[8-10]. The inert methyl group is prototype saturated aliphatic substituent with lipophilic and electron-donor inductive effect. It also behave as cognate group. The

numerical value imparts the steric bulk (voluminess). The Isopropyl and iso pentyl have less volume than t- butyl group. They are less bulky with maximal electrondonor inductive effect. Methyl groups have conformational effect, for favorable ligand- receptor interaction. N-methyl in peptide chain favors bioactive conformation and improves stability against enzymatic degradation.

The methylation of histamine at positions C-2 and C-4 has receptor selectivity profile. 2-methyl histamine is more active at HI-Rs than H2-Rs while 4-methyl histamine reversed this. Methyl group blocks the reactivity of OH, SH and NH2X groups.

The cyclopentyl has good fitting in hydrophobic pockets of target protein due to reasonable bulkiness and good replacement for gem-methyls. The gem-methyls and spiroisopropyeg, promote lipophilicity, metabolic stability, and symmetry.

The introduction of unsaturated groups (vinyl, allyl,ethnyl) in drug molecules have various effects.

- Impart geometrical isomerism.
- Induce lectron attracting inductive effect.
- Activation through conjugation (dienes, enyenes, polyunsaturated) enhances reactivity.
- Unsaturation plays role in drug action by addition to biological nucilophiles.

Unsaturation plays role in drug action by addition to biological nucilophiles. Unsaturation is vunerable site for metabolic blockade by epoxylation. The substituted vinyl group and cyclopropyl have reactivity comprise. Vinyl barbital, 17-alpha-vinyltestosterone, vigabartion are stable drugs. Vinylic epoxysides have anticancer application, by enhancing glutathione.

Allylic compounds are generally heptotoxic. They are C-allyl, N-allyl, O-allyl and S-allyl (isoteric) devatives. C-allyl is lipophilic and quickly metabolized, favoring rapid onset of action eg. Allobarbital, and short acting anaesthetics. N-Allyl induced antagonism in opiates by replacement of N-CHs. N-Allyl derivatives of hydantoins and dibenzoazepines have peripheral vasodilatory effect. O and S-allyls are isosteric groups. Analgesic, anti-inflammatory (Aclofenic) and beta blockers (oxprenolol) have quick onset of action and eliminatron benefits.

Acetylenic groups are useful for electronic effects and structural constrains. The equivalence to aryl ring gives electron attracting effect. Ethynyl compounds are hypnotic, sedative and orally effective contraceptives with steroidal structure. The ethnylated drugs (Na-methohexital, ethynyl estradiol) are rapidly metabolized and eliminated.

The Halogens have great structural values in SAR modifications. They exert three types of effects.

A. Steric effect- Halogen substitution can impose semi-rigidity by restricting sigma bond rotation for example Clonidine (antihypertensive) has bulky chlorine atoms which prevent free rotation and maintain the planes of aromatic rings in a 90° position to each other. Benzodiazepine receptor ligands have ortho and para isomers with similar lipophicity and electronic effects. The ortho-CI has reduced affinity due to steric effect.

B. Electronic effect- it is ascribed to inductive electron attracting effect which is maximal for chlorine, and moderate for bromine, and weak for iodine.

C. Hydrophobic effect- This effect is useful in general anaesthetics and antiseptics. There is direct correlation between biochemical activity and certain physical chemical parameters eg Pc, surface tension. F and CF3 have dramatic effect.

The cognate usefulness of halogens is related with reactivity and physicochemical properties. Fluorine and chlorine have maximal utilization in medicinal chemistry when attached to inert carbon (non-activated). Chlorine substituent increases lipophilicity, electron attracting inductive effect and metabolic obstruction. Bromine is not preferred due to its reactive toxicity. Iodine is essential for thyroidal activity. Iodine has hypersensitive side effects. Iodine has specific use in radiological contrastsubstances. Chlorine, CF, CN, N, groups are bioisosteric, so congate extensions are SCN, SCF S02 CF, and CH-CFs.

Hydroxylation adds OH by the replacement of hydrogen. Alcoholic and phenol groups alter the solubility of active molecules. They render hydrophicity with reduced Log P value. The Hansch value for hydroxyl group is 0.67. Ligand receptor- Interaction of hydroxalated drugs eg. Dopamine 5-HT, opiates and steroids form H- bonding with receptor. OH is essential element for H-bonding. Hydroxylation participate in drug metabolism. Metabolic hydroxylation of drug is also refered as detoxification.

Thiol (SH) and disulfide functions are essential parts of endogeneous biomolecules- proteins enzymes and hormones. They are highly reactive Drugs containing thiol groups have high affinity for heavy metals Methylthio and thioethers have therapeutical importance. Thiol binds to zinc containing enzymes, eg penicillamine for mode of action.

DISCUSSION AND RESULT[11-12]

The replacement of H in the structures of drugs by chemophorie groups is pharmaceutically is very essential for the pharmcokinetie and pharmacodyamic improvements. This replacement modifers act as of solubility, partition coefficient electron of density, steric environment bioavailability and interactions with target proteins.

The pharmacological vunerability of substituents is very important in analog design," for the SAR modifications. The acidic and basic groups of ionizable drugs have pka and pH values which effect unionized and ionized concentrations of the drug molecules. The acidic functions search cationic environment at receptor site where as basic groups move to anionic area.

The methyl defines hydrophobicity and modulates crystal lattice energy in aqueous medium. It has positive increment of 0.52 Hansch constant calculations. The steric hinderance is also attributed by the number of methyl groups. The SAR studies prefer methyl groups as electron donor. The anticancer drugs use methyl group as good leaving group

and generate electrophile (allylic cation) stabilized by reasonance CH, group has protective effect against metabolic hydroxylation. The antioxidative function of enc-diol in vitamin C is blocked by methylation as CHy group also behaves as cognate group.

Ionic drugs are precursors for prodrugs through esters amides and peptides formations to improve solubility and duration of action.

Unsaturated groups are reactive sites for drug design. Intrestingly saturated cyclopropyl is suitable subsituent for vinyl group as it prevents unstability and isomenzation. Ethynyl groups are biosteric to aromatic ring as aryl x electrons have small volumes. Acetylenic function is rigid with distance of 4.2 A° between two carbons eg.Oxotremorine (cholinergic agonist) Triple bond imposes rigidity, and an extension of electron donor- acceptor interaction.

Halogenated drugs have greater potential for potency F,CF3, and Cl are notable chemophoric and congate substituents. F has small vanderwaals radius, closer to H-atom therefore useful to block metabolically liable positions of drug molecules, thus enhance metabolic stability. CF; has size similar to chlorine, the replacement of chlorine by CF, activate carbon position.

The pharmacological analogs show similitude of electrostatic potential mapping. The aryl ring without (EPM) halogen substituent devoid of electronegativity. Fluoro aryl develops region of electronegative due to lone pair of fluoro electrons which generates electrostatic potential. The similitude of EPM allows the selection of substituent.

Alcoholic and phenolic groups have capacity to accept activated group through group- transferring enzymes (methylation, sulfnation etc.) for detoxification. Hydroxylation of OH changes solubility status of drugs. Thiol group maintains structural integrity as consolidates in peptidomimetics.

CONCLUSION

The pharmacological vunerability of chemophoric groups and their congation is haptophoric and pharmacophoric. The former is involved in binding affinity and later one in biological activity. Truly speaking chemophoric functions have biophoric nature[13] for interacting with biological targets.

ACKNOWLEDGEMENT

The author expresshis thankfulness to Prof. Veerma Ram (Vice Chancellor & Director of Pharmaceutical Sciences & Technology) for his worthy suggestions.

REFERENCES

1. Organic functional groups https://org.researchgate.net
2. Congate groups Wikipedia http://www.whoc-no/atc
3. Saxton, W.A. (1963) chemical constitutions and Biological Activity 3d edn, p. 103, E&F, N Spon, London.
4. Craig, P.N. (1980), Guideline for drug and analog design. In Wolf, M.E (ed.). The Basis of Medicinal Chemistry-Burge's Medicinal Chemistry, pp. 331-348. John Wiley, New York.
5. Lne, G.M>, Jr. and Johnson. M.R. (1967) Narcotic antagonists and analgesics, Annual Reports in Medicinal Chemistry, pp. 22-32 Academic Press, New York.
6. R. (eds), ActualitesPhamacologiques, pp.221-243, Masson Paris.
7. Chu, K.C. (1980) The quantitive analysis of structure activity relationships,In Wolf, M.E (ed.). The Basis of Medicinal Chemistry/Burger's Medicinal Chemistry, pp. 393-418, John Wiley, New York.
8. Rekker, R.F. and Manhold, R. (1992) Calculation of Drug Lipophilicity, Verlag VCH, Weinheim, Germany.
9. Nemethy, G. (1967) Hydrophobic interactions, Angew. Chem. Int. Ed. Eng.6: 195-206..
10. Hansch, C. and Anderson, SM. (1967) The effect of intramolecular hydrophobic bonding on partition coefficients. J. Org. Chem. 32:2583-2586.
11. Martin, Y.C. (1978) Quantitative Drug Design. A Critical Introduction, Dekker, New York.
12. Ganellin, C.R. and Roberts: SM. (1993) Medicinal Chemistry. The Role of Organic Chemistry in Drug Research, 2 edn. Academic Press, London.