

- BCG - Vaccine Lab. → Madras/Chennai
- Central Drug Testing Lab (CDTL) → Bombay
- Central Drug Laboratory (CDL) → Calcutta → Biological & Microbiological
- Central Drug Research Institute (CDRI) → Lucknow
- Central Research Institute (CRI) → Kasauli → Gene, Antigen, Vaccine
- Indian Drug Mfrs. Association (IDMA) → Bombay
- Indian Society of Blood Transfusion & Immunohaematology → Pune
- Indian Veterinary Research Institute - I 33 at nagar
- Central Indian Pharmacopoeia Laboratory (CIP) - Ghaziabad → Condens
- National Plasma Fractionation Centre - Bombay
- National Institute of Communicable Disease - New Delhi → Polio Vaccine
- National Institute of Virology - Pune
- Organisation of P'cal Producers (OPPI) - Bombay
- Dabur Research Foundation - Ghaziabad.
- Ministry of Defence - Kanpur
- WHO - Geneva.
- BP. Commission - London
- AIIMS - New Delhi
- Tata Memorial Hospital - Bombay
- Kothari Medical Centre → Calcutta.
- University College of Medical Sciences & Guru Teg Bahadur Hospital → Delhi

Delhi → National Institute of Communicable Disease
 → AIIMS → Guru Teg Bahadur Hospital → Inst. of Applied Manpower Research

Bombay → CD Testing Lab. → IDMA → National Plasma Fract. Centre
 → Org. of P'cal Producers (OPPI) → Tata Memorial Hospital

Madras → BCG-Vaccine Lab.

Calcutta → CD Lab., Kothari Medical Centre

Lucknow → CDRI // Kasauli → CRI

Ghaziabad → Central Indian P'copeia Lab., Dabur

Pune → Indian Soci. of Blood Transfusion & Immunohaematology
 National Inst. of Virology

I 33 at nagar → Indian Veterinary Research Institute

Kanpur → Ministry of Defence

→ Synthetic Drug Plant → Hyderabad. (IDPL)

IP-1946 from BP-1932.

National P'cal Pricing Authority (NPPA)
 - Aug - 1997

* Jury :-

- Poison Act → 1919 // Opium Act - 1857, 1878
- Dangerous Drug Act - 1930
- Drug Act - 1940 , Drug rules - 1945
- Pharmacy Act - 1948
- Advisory Board - DTAB to DCC → Drug Technical Advisory Board to Drug Consultative Committee

Pre-constitution → Opium Act - 1857, 1878 // Poison Act - 1919
Dangerous Drug Act - 1930 // Drug Act - 1940.

- Post-constitution → Pharmacy Act - 1948, Drug & Magic Remedies (Objectionable Advertisement) - 1954
- Medicinal & Toilet Prepⁿ (Excise Duties) - 1955, 1976 → Ethanol
 - The Drugs (Price Display & Control) Order - 1966 → 70-6987-95
↳ 1962 - revised
 - Insecticides Act - 1968
 - Medical Termination of Pregnancy Act - 1971 → 75 → EXCISE
↳ 1972 - revised
 - Narcotic Drugs & Psychotropic Subs. Act - 1985
 - Drug & Cosmetic Act - 1940
 - Drug Policy - 1986. / Patent Act - 1970-72-99

PCI → Elected - Six ⇒ UGC - (Pharmacy, P. chem., cogno., cology)
↳ 1 - MCI, 1 - State Council.

Nominated - Six ⇒ UGC representative & AICTE (1987)
↳ State Govt.

Ex-officio ⇒ Director General of Health Services,
Director - CDL, Drug Controller of India

* Cosmetic Colour → 2 ppm - Arsenic, 20 ppm - Lead
100 ppm - Heavy Metal.

- * Schedule - G → Cancer, Diuretic, Oral hypoglycaemic, Hydantoin, Insulin, Antihistaminic
- * Schedule - O → Grade - 1 (18), 2 (10), 3 (05)
- * Sch - F → Vaccines, Toxins, Antigens & Sera.
- * Sch - W → Generic Names → Analgin, FeSO₄, Aspirin, Piperazines, Chlorpromazine
- * Sch - M & Y → 1988

QSAR

Corwin Hansch → 1964 → SAR in Quantitative terms.

- Cram-Brown & Fraser → 1868 → Curare → $H^+ - NH_4^+$
- Richardson → Aliphatic alcohol → mol. wt. → Hypnotic.
- Meyer & Overton → Insecticidal → Boiling point
- Narcotic → Surface Tension (K_{ow})

* QSAR Methods:- (I) Free-Energy Models.

- (a) Hansch method - Linear Free Energy relationship
- (b) Martin & Kubinyi - non-linear
- (c) Free-Wilson Mathematical model.

(II) Other Statistical Methods -

- (a) Discriminant Analysis → Yvonne Martin-1974 (1 or 0)
- (b) Principal Component Analysis
- (c) Factor Analysis
- (d) Cluster Analysis → $P < 0.05$
- (e) Combined Multivariate Analysis

(III) Pattern Recognition

(IV) Topological Method → Steric misfit & receptor (MTD)

(V) Quantum Mechanical Method

(VI) Molecular Modelling

* Increase in Entropy Leads to stabilization of drug-receptor complex. ∝ to nonpolar part of drug's surface Area.

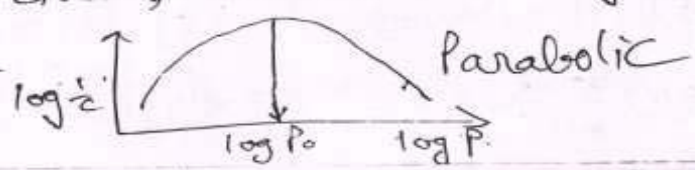
* 1-octanol ⇒ 1.7 M water ⇒ Low Vapour Pressure
 ⇨ UV-transparent.

⇒ Negative π -value → prefer aqueous phase
 Positive π -value → prefer organic phase

⇒ $\log \frac{1}{c} = a \log P + b$ [Linear Relationship]

↳ Activity ↑ ∝ ↑ in lipophilicity
 eg:- protein binding drugs, unspecific toxic, anaesthetic, bactericidal, fungicidal, narcotic, hemolytic, phenyl ethylamines

⇒ Non-Linear



$R_m = \log \left(\frac{1}{k_f} - 1 \right) \rightarrow$ not true equilibrium parameter

ortho effect \rightarrow o-disubstituted leads to low log P & π -value

$\Delta \pi$ -ortho = (π O-subst) - (π P-subst.)

MV = $\frac{\text{mol. wt.}}{\text{density}}$

$M_R = \frac{n^2-1}{n^2+2} \cdot \frac{\text{mol. wt.}}{\text{density}} \Rightarrow PA = R^{\frac{1}{4}} \frac{\text{mol. wt.}}{\text{density}}$

$\left. \begin{matrix} \text{refractivity} \\ \text{volume term} \end{matrix} \right\} \text{ or } \left. \begin{matrix} \text{electron} \\ \text{polarisability} \end{matrix} \right\} \rightarrow$ measure of dispersion & dipole-induced dipole forces.

M_R & Parachor are corrected molar volumes

Capacity Factor by HPLC = $k' = \frac{t_r - t_0}{t_0}$

logarithmic of constant $\Rightarrow \pi$ -value.

Electronic Parameter

Hammett constant \rightarrow HC Brown constant (σ_p)
 \rightarrow benzoic a, anilines, phenols \rightarrow dimethylphenyl-carbonyl chlorides.

Molar effect (σ_M) \rightarrow Mesomeric effect (σ_R)

Luft's polar substituent constant (σ^*) \Rightarrow aliphatic ester hydrolysis

Homolytic Constant (\Rightarrow free-radicals.)

Field & Resonance component (F & R) ($\sigma_m \pm \sigma_p$)

$n^2 = \frac{(n^2-1)m}{(n^2+2)d} \leftarrow$ Lorenz-Lorenz

$\log k_a = 4.2 - 1.00 \sum \sigma \leftarrow$ Hammett eqⁿ.

More Negative $\sigma \Rightarrow e^-$ -releasing nature of substituent

Luft's Constant = $E_s = \log \left(k/k_0 \right)$

$\text{CH}_3 = \text{Zero}$ \rightarrow Intramolecular steric effects

M_R, van der Waals radii, mol. wt.

Molecular connectivity index (X) (indicates degree of branching)
 \rightarrow molecular substructures in Topological terms

\rightarrow lipophilicity & Steric features.

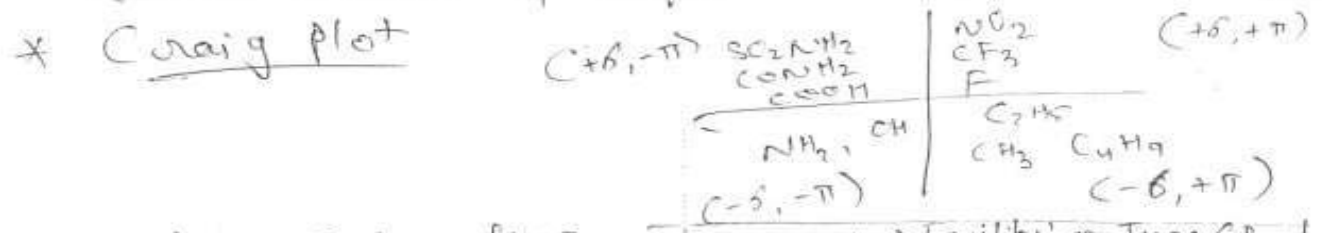
e^- drawing inductive effect \Rightarrow \downarrow H-bonding

\Rightarrow \uparrow lipophilicity \Rightarrow \uparrow log P & π -values.

Gaussian eqⁿ \rightarrow Rate of drug actⁿ = $A = f(\log P) = a \cdot \exp \left[- \frac{(\log P - \log P_0)^2}{b} \right]$

$\# \rightarrow$ Hirsch model $\Rightarrow \log \frac{1}{\nu} = k_1 \pi + k_2 \delta + k_3 E_s + X$
 \rightarrow Free-Wilson $\Rightarrow \log \frac{1}{\nu} = \mu + \sum a_{ij}$
 \rightarrow Mixed (Kubinyi) $\Rightarrow \log \frac{1}{\nu} = \sum a_{ij} + \sum k_j \phi_j + K$

- * $(+\pi) \leftrightarrow (-\delta) \Rightarrow e^-$ -releasing groups
- * $(-\pi) \leftrightarrow (+\delta) \Rightarrow e^-$ -withdrawing groups
- * Topliss Approach \Rightarrow Also Craig plot, Fibonacci search method & Sequential Simplex Strategy.



- * Bonding Interactions
 - stretching, Bending & Torsional (NMR)
 - Equilibrium Type (Bond angle, length) \rightarrow X-ray, neutron or e^- diffraction
 - Force Constant Type \rightarrow IR
- * Non-Bonding Interactⁿ:
 - Dispersive attractⁿ (van der Waal), - dipole-dipole interactⁿ,
 - charge-charge interactⁿ \Rightarrow London, Coulomb.

* Molecular Dynamics

- Monte Carlo method
- Molecular dynamic method.

$$X = \frac{\sum_i x_i \exp(-E_i/KT)}{\sum_i \exp(-E_i/KT)}$$

- * Quantum Mechanics:
 - Schrodinger Eqⁿ method - Extended Huckel method.
 - Complete Neglect of Differential Overlap (CNDO)
 - Intermediate Neglect (INDO)
 - Modified Intermediate (MINDO)
 - Neglect of Diatomic Differential Overlap (NDDO)
 - Modified NDDO (MNDO)

- * CoMFA (Comparative Molecular Field Analysis) \rightarrow 3.D
- * Simulated Annealing * Neural Networks
- * Contour Plots (CoMFA) * Pharmacophore Mapping \rightarrow Dock
- * MSA-Molecular Shape Analysis \rightarrow Common Overlap Steric Volume - COSY