Glossary

3D QSAR QSAR studies which relate the biological activities of a series of compounds to their steric and electrostatic fields determined by molecular modelling software.

Abzyme An antibody with catalytic properties.

ACE inhibitors Drugs which inhibit the enzyme angiotensin converting enzyme. Inhibition prevents the synthesis of a powerful vasoconstrictor and so ACE inhibitors are used as antihypertensive agents.

Acetylcholinesterase An enzyme that hydrolyses the neurotransmitter acetylcholine.

Action potential Refers to the reversal in membrane potential as a signal travels along the axon of a neuron.

Activation energy The energy required for a reaction to reach its transition state.

Active conformation The conformation adopted by a compound when it binds to its target binding site.

Active principle The single chemical in a mixture of compounds which is chiefly responsible for that mixture's biological activity.

Active site The binding site of an enzyme where a reaction is catalysed by the enzyme.

ADAPT Antibody-directed abzyme prodrug therapy.

Addiction Addiction can be defined as a habitual form of behaviour. It need not be harmful. For example, one can be addicted to eating chocolate or watching television without suffering more than a bad case of toothache or a surplus of soap operas.

ADEPT Antibody directed enzyme prodrug therapy

ADME Refers to drug absorption, drug distribution, drug metabolism and drug excretion.

Adrenal medulla A gland that produces adrenaline.

Adrenergics Refers to compounds that interact with the receptors targeted by adrenaline and noradrenaline.

Adrenoceptors Receptors that are activated by adrenaline and noradrenaline.

Adsorption Refers to the situation where a molecule or a structure adheres to a surface. In virology it refers to a virus binding to the surface of a host cell.

Aerobic bacteria Bacteria that grow in the presence of oxygen.

Affinity Affinity is a measure of how strongly a ligand binds to its target binding site.

Affinity screening A method of screening compounds based on their binding affinity to a target.

Agonist A drug that produces the same response at a receptor as the natural messenger.

AIDS Acquired immune deficiency syndrome.

Alchemy A molecular modelling softwear package.

Alkaloids Natural products extracted from plants that contain an amine functional group.

Alkylating agents Agents that act as electrophiles and form irreversible covalent bonds with macromolecular targets. These agents are classed as cytotoxic and are used as anticancer agents.

Allosteric Refers to a protein binding site other than the one used by the normal ligand, and which affects the activity of the protein. An allosteric inhibitor binding to an allosteric binding site induces a change of shape in the protein which disguises the normal binding site from its ligand.

Aminoacridines A group of synthetic antibacterial agents that target bacterial DNA.

Aminoacyl tRNA synthetases Enzymes that catalyse the attachment of an amino acid to transfer RNA. Potentially useful targets in antibacterial therapy.

Aminoglycosides A group of antibacterial agents that contain sugar components and a basic amino function.

Anaerobic bacteria Bacteria that grow in the absence of oxygen.

Anchor *see* linker.

Androgens Hormones that are used in anticancer therapy.

Angiogenesis The process by which new blood vessels are formed.

Angiostatin An endogenous compound that inhibits angiogenesis.

Anomers Cyclic stereoisomers of sugars that differ only in their configurations at the hemiacetal (anomeric) carbon.

Antagonist A drug which binds to a receptor without activating it, and which prevents an agonist or a natural messenger from binding.

Antedrugs *see* Soft drugs.

Anthracyclines A group of antibiotics that are important in anticancer therapy.

Antiandrogens Anticancer agents that block the action of androgens at their receptors.

Antibacterial agent A synthetic or naturally occurring agent which can kill or inhibit the growth of bacterial cells.

Antibiotic An antibacterial agent derived from a natural source.

Antibody A 'Y' shaped glycoprotein that is generated by the body's immune system to interact with an antigen present on a foreign molecule. Marks the foreign molecule for destruction.

Antibody–drug conjugates Refers to antibodies with drugs covalently linked to their structure.

Anticholinesterases Agents which inhibit the enzyme acetylcholinesterase.

Anticodon A set of three nucleic acid bases on transfer RNA that base pair with a triplet of nucleic acid bases on messenger RNA during translation. The amino acid linked to tRNA is determined by the anticodon that is present.

Antiemetic A drug used to prevent nausea and vomiting.

Antigen A region of a molecule that is 'recognized' by the body's immune system and which will interact with antibodies targeted against it.

Antigenic drift The process by which antigens gradually vary in nature.

Antigenic shift Refers to a large alteration in the nature of antigens.

Antigenic variation A property of some viruses that are able to vary the chemical structure of antigens on their surface through rapid mutations.

Antimetabolites Agents which inhibit enzymes that are crucial to the normal metabolism of the cell. Used in antibacterial and anticancer therapy.

Antioestrogens Agents which bind to oestrogen receptors and block oestrogen. Used in anticancer therapy.

Anti-oncogenes Genes that code for proteins which check the 'normality' of a cell and which induce cell death if abnormalities are present. Important in preventing the birth of a cancer cell.

Antisense therapy The design of molecules which will bind to specific regions of m-RNA and prevent the m-RNA acting as a code for protein synthesis.

Aorta The principle artery carrying blood away from the heart.

Apaf-1 A scaffolding protein for apoptosomes.

Apoptosis The process by which a cell commits suicide.

Apoptosome A protein complex that destroys the cell's proteins and leads to apoptosis.

Aquaporins Membrane bound proteins containing a pore that allows water to pass through the membrane.

Aromatase and aromatase inhibitors An enzyme that catalyses an aromatization reaction in oestrogen synthesis. Inhibitors are used as anticancer agents.

Arteries Blood vessels taking blood away from the heart.

Aspartyl proteases Enzymes that catalyse the hydrolysis of peptide bonds in protein substrates and which contain aspartate residues in the active site that take part in the hydrolysis mechanism.

Asymmetric centre An atom with four different substituents that frequently results in asymmetry for the whole molecule.

Asymmetric synthesis A synthesis which shows selectivity for a particular enantiomer or diastereomer of an asymmetric compound.

Attention deficit hyperactivity disorder A disorder associated with children—the name speaks for itself!

AUC Stands for area under the plasma drug concentration curve. It represents the total amount of drug that is available in the blood supply during a dose regimen.

Autonomic motor nervous system Nerves carrying messages from the central nervous system to smooth muscle, cardiac muscle and the adrenal medulla.

Bacilli Bacterial cells that are rod shaped.

Bacteriostatic Bacteriostatic drugs inhibit the growth and multiplication of bacteria, but do not directly kill them.

Bactericidal Bactericidal drugs actively kill bacterial cells.

Bacteriophage A virus that invades bacterial cells.

Bad A protein that promotes apoptosis.

Barbiturates A series of synthetic compounds with sedative properties.

Bax A protein that promotes apoptosis.

Bcl-2 and Bcl-X Proteins that suppress apoptosis.

Benign cancer or tumour A localized tumour that is not life threatening.

Benign prostatic hyperplasia The term for an enlarged prostate, resulting in difficulty in passing urine.

Beta-blockers Refers to series of compounds that block or antagonize β-adrenoceptors. Particularly useful in cardiovascular medicine.

Beta-lactamase inhibitors Agents which inhibit the beta-lactamase enzymes.

Beta-lactamases *see* lactamases.

Bile duct A duct leading from the liver to the intestines. Some drugs and drug metabolites are excreted through the bile duct, but can be reabsorbed from the intestines.

Binding region A region within a binding site that is capable of interacting with a drug or an endogenous molecule by intermolecular bonding.

Binding site The location where an endogenous molecule or drug binds on a macromolecule. Normally a hollow or cleft in the surface of the macromolecule.

Bioavailability Refers to the fraction of drug that is available in the blood supply following administration.

Bioequivalence studies Studies carried out to ensure that the bioavailability of a drug remains the same should there be any alteration to the manufacture or formulation of the drug.

Bioisostere A chemical group which can replace another chemical group without affecting the biological activity of the drug.

Bioterrorism The use of toxic infectious agents by terrorist groups.

Bleomycins A group of naturally occurring glycoproteins used as anticancer agents.

Blood–brain barrier Blood vessels in the brain are less porous than blood vessels in the periphery. They also have a fatty coating. Drugs entering the brain have to be lipophilic in order to cross this barrier.

Boc A short hand term for the protecting group, t-butyloxycarbonyl.

Bronchodilator An agent which dilates the airways and can combat asthma.

Bump filter Used in conformational analysis *in silico* to reject conformations that have bad steric interactions.

Cache A molecular modelling software package.

Calmodulin A calcium binding protein that activates several protein kinases.

Camptothecins A group of naturally occurring alkaloids and semi-synthetic derivatives used as anticancer agents.

Canaliculae Invaginations or channels formed by parietal cells which connect with the lumen of the stomach.

Capillaries Small blood vessels.

Carboxypenicillins A family of penicillins having a carboxylic acid substituent at the α-position, which have been largely superseded.

Capsid A protein coat that encapsulates the nucleic acid of a virus.

Carbapenems A group of β-lactam antibacterial agents, so called because they lack a sulfur atom.

Carboxypeptidases Enzymes that hydrolyse the final peptide link at the *C*-terminal end of a peptide chain.

Carcinogenesis The birth of a cancer.

Carrier protein A protein in the membrane of a cell which is capable of transporting specific polar molecules across the membrane. The molecules transported are too polar to cross the membrane themselves and are crucial to the survival and functions of the cell.

Caspases Enzymes which have important roles to play in the ageing process of cells.

Catecholamines Compounds that contain a basic amino group and a catechol ring. The catechol ring consists of an aromatic ring with two phenolic groups, *ortho* to each other.

Cell cycle Refers to recognizable phases of cell growth, DNA synthesis and cell division.

Cell membrane A phospholipid bilayer surrounding all cells that acts as a hydrophobic barrier.

Central nervous system The nerves that are present in the brain and the spinal column.

Centroid A dummy atom used in molecular modelling to define the centre of an aromatic or heteroaromatic ring. Has also been used to mean the scaffold of a molecule.

Cephalosporinases *see* lactamases.

Cephalosporins A group of β-lactam semi-synthetic antibacterial agents that target the bacterial transpeptidase enzymes.

Cephamycins A family of cephalosporins having a methoxy substituent at the 7-position.

Chain cutters Agents that interact with DNA, leading to the splitting of the DNA backbone. Generally operate by producing radicals. Used as anticancer agents.

Chain contraction/extension strategy The variation of chain length in a drug to optimize the separation between different binding groups.

Chem 3D A molecular modelling softwear package.

ChemDraw A chemical drawing softwear package.

ChemWindow A chemical drawing softwear package.

Chem-X A molecular modelling softwear package.

Chemotherapeutic index A comparison of the minimum effective dose of a drug with the maximum dose which can be tolerated by the host.

Chimeric antibodies Antibodies that are part human and part mouse in nature.

Chirality The property of asymmetry where the mirror images of a molecule are non-superimposable.

Chiral switching The replacement of a racemic drug on the market with its more active enantiomer or stereoisomer.

CHO cells Stands for Chinese Hamster Ovarian cells. Commonly used to express a cloned receptor on their surface for *in vitro* tests.

Choline acetyltransferase An enzyme that catalyses the synthesis of acetylcholine.

Cholinergics Refers to compounds that interact with cholinergic receptors.

Cholinergic receptors Receptors that are activated by acetylcholine.

Chromatin A structure consisting of DNA wrapped round proteins such as histone.

Cloning The process by which identical copies of a DNA molecule or a gene are obtained.

CMV *see* cytomegalovirus.

Cocci Bacterial cells that are spherical in shape.

Coenzyme The name given to small organic molecules acting as cofactors.

Cofactor Cofactors are ions or small organic molecules (other than the substrate), which are bound to the active site of an enzyme and take part in the enzyme catalysed reaction.

Combinatorial libraries A store of compounds that have been synthesised by combinatorial synthesis.

Combinatorial synthesis A method of synthesizing large quantities of compounds in small scale using automated or semi-automated processes. Normally carried out as solid phase syntheses.

Combretastatins Naturally occurring anticancer agents that inhibit tubulin polymerization.

Comparative molecular field analysis (CoMFA) A method of carrying out 3D QSAR that was developed by the company Tripos.

Competitive inhibitors Reversible inhibitors that compete with the normal substrate for an enzyme's active site.

Compound banks or libraries A store of synthetic compounds that have been produced by traditional methods or by combinatorial syntheses.

Conformational analysis A study of the various conformations permitted for a molecule. Conformations are different three dimensional shapes arising from single bond rotations.

Conformational blockers Groups that are added to molecules to prevent them adopting certain conformations.

Conformational space The three-dimensional space surrounding the scaffold of a molecule.

Conjugation In the chemical sense it refers to interacting systems of pi bonds. In the microbiological sense, it refers to the process by which bacterial cells pass genetic information directly between each other.

Conjugation reactions *see* phase II reactions.

Convergent evolution Refers to the receptors which are in different branches of the receptor evolutionary tree, but which have converged to recognize the same endogenous ligand.

Correlation coefficient *see* regression coefficient.

Cotransmitters Chemical messengers which are released from neurons along with the major neurotransmitter and which have a 'fine tuning' effect on the signal received.

Craig plot A plot which compares the values of two physicochemical parameters for different substituents.

Cross-validated correlation coefficient (q2) A measure of the predictability of a 3D QSAR equation.

Cross validation Used in 3D QSAR in order to obtain a QSAR equation. Tests how an equation predicts the activity of a test compound that has not been included in the derivation of the equation.

Cryptophycins Naturally occurring anticancer agents that inhibit tubulin polymerization.

Cyclases Enzymes that catalyse cyclisation reactions such as the formation of cyclic AMP from ATP.

Cyclin dependent kinases Enzymes that are activated by cyclins and which catalyse phosphorylation reactions that control the cell cycle.

Cyclins A group of proteins that are important in the control and regulation of the cell cycle.

Cyclo-oxygenases Enzymes that are important in the production of prostaglandins.

CYP Short-term nomenclature for cytochrome P450 enzymes; for example CYP3A4.

Cytochrome c Released by mitochondria to promote apoptosis.

Cytochrome P450 enzymes Enzymes that are extremely important in the metabolism of drugs. They catalyse oxidation reactions.

Cytomegalovirus A virus that causes eye infections and blindness.

Cytoplasm The contents of a cell.

Cytotoxic agents Anticancer agents that are generally toxic to cells by a number of mechanisms.

Database mining The use of computers to automatically search databases of compounds for structures containing specified pharmacophores.

***De novo* drug design** The design of a drug or lead compound based purely on molecular modelling studies of a binding site.

Death activator proteins Chemical messengers that trigger a cell to commit suicide.

Deconvolution The isolation and identification of an active compound in a mixture of compounds obtained from a combinatorial synthesis.

Dependence A compulsive urge to take a drug for psychological or physical needs. The psychological need is usually why the drug was taken in the first place (to change one's mood) but physical needs are often associated with this. This shows up when the drug is no longer taken leading to psychological withdrawal symptoms (feeling miserable) and physical withdrawal symptoms (headaches, shivering, etc.) Dependence need not be a serious matter if it is mild and the drug is non-toxic (e.g. dependence on coffee). However, it is a serious matter if the drug is toxic and/or shows tolerance. Examples: opioids, alcohol, barbiturates, diazepams.

Desensitization The process by which a receptor becomes less sensitive to the continued presence of an agonist.

Desolvation A process that involves the removal of surrounding water from molecules before they can interact with another; for example a drug with its binding site. Energy is required to break the intermolecular interactions involved.

Differentiation The ability of cells to become specialized in a multicellular organism.

Dihydrofolate reductase and dihydrofolate reductase inhibitors An enzyme involved in generating tetrahydrofolate—an important enzyme cofactor. Inhibitors prevent the synthesis of nucleic acids and are used as antibacterial and anticancer agents.

Dipole–dipole interactions Interactions between two separate dipoles. A dipole is a directional property and can be represented by an arrow between an electron rich part of a molecule and an electron deficient part of a molecule. Different dipoles align such that an electron rich area interacts with an electron deficient area.

Discovery Studio Pro A molecular modelling softwear package.

Displacer A test compound that competes with a radioligand for the binding site of a receptor.

Divergent evolution Refers to the divergence of receptors with evolution. Receptor that diverged early in evolution have greater differences in their binding sites and ligand preferences.

DNA Deoxyribonucleic acid.

DNA ligase An enzyme that repairs breaks in the DNA chain.

DNA polymerases Enzymes that catalyse the synthesis of DNA from a DNA template.

DNA viruses Viruses that contain DNA as their nucleic acid.

DOCK A software program used for docking molecules into target binding sites.

Docking The process by which a molecular modelling program fits a molecule into a target binding site.

Dose ratio The agonist concentration required to produce a specified level of effect when no antagonist is present, compared with the agonist concentration required to produce the same level in the presence of an antagonist.

Drug–drug interactions Related to the effect one drug has on the activity of another if both drugs are taken together.

Drug load The ratio of active drug in the total contents of a dose.

Drug metabolism The reactions undergone by a drug when it is in the body. Most metabolic reactions are catalysed by enzymes, especially in the liver.

dsDNA Double-stranded DNA. A term used in virology.

dsRNA Double-stranded RNA. A term used in virology.

Dummy atom *see* centroid.

Dynamic combinatorial chemistry The generation of a mixture of products from a mixture of starting materials in the presence of a target. Products are in equilibrium with starting materials and the equilibrium shifts to products binding to the target.

Dynamic structure–activity analysis The design of drugs based on which tautomer is preferred for activity.

Dynorphins Endogenous polypeptides that act as analgesics

E_s *see* Taft's steric factor

EC_{50} The concentration of drug required to produce 50% of the maximum possible effect.

ED_{50} The mean effective dose of a drug necessary to produce a therapeutic effect in 50% of the test sample.

Efficacy Efficacy is a measure of how effectively an agonist activates a receptor. It is possible for a drug to have high affinity for a receptor (i.e. strong binding interactions) but have low efficacy.

Electronic screening *see* database mining.

Electrostatic interactions *see* ionic interactions.

EMEA *see* European agency for the evaluation of medicinal projects.

Enantiomers Refers to the mirror image forms of an asymmetric molecule having one asymmetric centre.

Endocytosis The process by which a segment of cell membrane folds inwards and is 'nipped off' to form a vesicle within the cell.

Endogenous Endogenous compounds are chemicals which are naturally present in the body.

Endomorphins Endogenous tetrapeptides that act as analgesics.

Endorphins Endogenous polypeptides that act as analgesics.

Endoplasmic reticulum Folds of membrane within eukaryotic cells. Endoplasmic reticulum can be defined as smooth and rough due to its appearance under the electron microscope. Rough endoplasmic reticulum has ribosomes attached to it and is where protein synthesis takes place.

Endpoint Used in clinical trials to determine whether a drug is successful or not. Some form of measurable effect.

Energy minimization An operation carried out by molecular modelling software to find a stable conformation of a molecule.

Enkephalinases Enzymes which hydrolyse enkephalins.

Enkephalins Endogenous peptides which act as analgesics.

Enteric nervous system Located in the walls of the intestine. Responds to the autonomic nervous system and local hormones.

Enzyme A protein that acts as a catalyst for a reaction.

Epimerization The inversion of an asymmetric centre.

Epitopes Small molecules that bind to part of a binding site and do not produce a biological effect as a result of binding.

Epothilones Naturally occurring anticancer agents that inhibit tubulin depolymerization.

Eukaryotic cell The cells that are present in plants, animals and multicellular organisms. They contain a membrane bound nucleus and organelles.

European patent convention (EPC) A group of European countries for which patents can be drawn up based on a European patent.

European agency for the evaluation of medicinal projects The European regulatory authority for the testing and approval of drugs.

European patent office (EPO) Issues European patents.

Exocytosis The process by which vesicles within a cell fuse with a cell membrane and release their contents out of the cell.

Extension strategies The addition of functional groups to a drug with the aim of achieving a further binding interaction with another binding region in the binding site.

F A symbol used in pharmacokinetic equations to represent oral bioavailability. Alternatively, a symbol used in QSAR equations to represent the inductive effect of a substituent.

Farnesyl transferase An enzyme that attaches a farnesyl group to the Ras protein to allow membrane attachment.

Fast tracking A method of pushing a drug through clinical trials and the regulatory process as quickly as possible. Applied to drugs that show distinct advantages over current drugs in the treatment of life threatening diseases, or for drugs that can be used to treat diseases that have no current treatment.

FDA *see* food and drugs administration.

Feedback control The process by which the product of an enzymatic reaction or a series of enzymatic reactions controls the level of its own production.

FGF *see* fibroblast growth factor.

Fibroblast growth factor A growth factor that stimulates angiogenesis.

Fight or flight response Refers to the reaction of the body to situations of stress or danger, and which involves the release of adrenaline and other chemical messengers that prepare the body for physical effort.

First pass effect The first pass effect refers to the extent to which an orally administered drug is metabolized during its first passage through the gut wall and the liver.

Fischer's lock and key hypothesis *see* Lock and key hypothesis.

Fisher's F-test A statistical test used to assess the significance of coefficients in a QSAR equation.

Flagellum A tail like structure used by some microorganisms as a method of propulsion.

Fluoroquinolones A group of synthetic antibacterial agents.

Fmoc A short hand term for the protecting group, 9-fluorenylmethoxycarbonyl.

Food and drugs administration (FDA) The drugs regulatory authority for the USA.

Force field Relevant to molecular modelling. Refers to the calculation of the interactions and energies between different atoms resulting from bond stretching, angle bending, torsional angles and non-bonded interactions.

Free–Wilson approach A QSAR equation which uses indicator variables rather than physicochemical parameters.

G-Proteins Membrane bound proteins consisting of three subunits which are important in the signal transduction process from activated G-protein coupled receptors.

G-Protein coupled receptors Membrane bound receptors that interact with G-proteins when they are activated by a ligand.

Gastrointestinal tract Consists of the mouth, throat, stomach and the upper and lower intestines.

Gating The mechanism by which ion channels are opened or closed.

GCP *see* Good clinical practice.

GDEPT Gene directed enzyme prodrug therapy.

Genomics The study of the genetic code for an organism.

Glomerulus A knotted arrangement of blood vessels which fits into the opening of a nephron and from where water and small molecules are filtered into the nephron.

Global energy minimum The most stable conformation of a molecule.

GLP *see* Good laboratory practice.

Glucocorticoids Hormones that are used in anticancer therapy.

Glycoconjugate The general term for macromolecules that are linked to carbohydrates.

Glycolipid A lipid molecule linked to one or more carbohydrates.

Glycomics The study of carbohydrates.

Glycopeptides and glycoproteins Peptides and proteins that are linked to one or more carbohydrates.

Glycopeptide antibacterial agents Glycopeptides with antibacterial, the most important being vancomycin.

Glycosidases Enzymes that catalyse the hydrolysis the glycosidic bond between carbohydrate groups.

Glycosphingolipids Glycoconjugates that are thought to be important in the regulation of cell growth. Includes the molecules responsible for labelling blood cells.

GMP *see* Good manufacturing practice.

Gonadotrophin-releasing hormone *see* Luteinizing hormone-releasing hormone.

Good clinical practice (GCP) Scientific codes of practice that apply to clinical trials and which are monitored by regulatory authorities.

Good laboratory practice (GLP) Scientific codes of practice that apply to a pharmaceutical company's research laboratories and which are monitored by regulatory authorities.

Good manufacturing practice (GMP) Scientific codes of practice that apply to a pharmaceutical company's production plants and which are monitored by regulatory authorities.

Granzyme An enzyme introduced into defective cells by T-lymphocytes, and which induces apoptosis.

GRID A molecular modelling software program that maps the nature of binding regions within a binding site.

Group shifts Refers to the transposition of a group within a molecule to make it unidentifiable to metabolic enzymes but not to target binding sites.

Growth factors Hormones that activate membrane bound receptors and trigger a signal transduction pathway leading to cell growth and division.

HAART Highly active antiretroviral therapy. A combination therapy used to treat HIV infections.

Half-life The time taken for the plasma concentration of a drug to fall by half.

HAMA response Stands for Human Anti-Mouse Antibodies. These are antibodies that are produced against monoclonal antibodies which have been derived from a mouse source, and are recognized as foreign by the body's immune system.

Helicases Enzymes that catalyse the coiling and uncoiling of DNA.

Hammett substituent constant (σ) A measure of whether a substituent is electron withdrawing or electron donating and to what extent.

Hansch equation A QSAR equation involving various parameters.

Hard drugs Refers to drugs that are resistant to metabolism.

HBA *see* hydrogen bond acceptor.

HBD *see* hydrogen bond donor.

Helicobacter pylori An organism that can survive in the stomach and cause damage to the stomach lining, leading to ulcers.

Haemagglutinin A glycoprotein on the surface of the flu virus that is crucial to the infection process.

Henderson–Hasselbalch equation An equation that is used to determine the extent of ionisation of an ionizable drug at a particular pH.

Herpes Viruses responsible for cold sores and other herpes infections.

High throughput screening An automated method of carrying out a large number of *in vitro* assays on small scale.

Histone acetylase and histone deacetylase Enzymes that acetylate and deacetylate the lysine residues of the structural protein, histone. Important in the control of gene expression.

HIV Human immunodeficiency virus.

HOMO Highest occupied molecular orbital.

Homology models A term used in molecular modelling for a the construction of a model protein or binding site based on the structure of known proteins or binding sites.

Hormones Endogenous chemicals that act as chemical messengers. They are typically released from glands and travel in the blood supply to reach their targets. Some hormones are local hormones and are released from cells to act in the immediate area around the cell.

Houghton's tea bag procedure A manual method of carrying out combinatorial synthesis.

HRV *see* Human rhinoviruses.

Human genome project The sequencing of human DNA.

Human rhinoviruses RNA viruses responsible for the common cold.

Hybridization Refers to the mixing of atomic orbitals to form hybridized atomic orbitals. With atoms such as carbon, nitrogen and oxygen, it involves the mixing of 2s and 2p orbitals to produce sp, sp^2 or sp^3 hybridized orbitals. Important as to whether the atoms concerned can form π bonds.

Hybridomas Cells that are formed from the fusion of B-lymphocytes with immortal B-lymphocytes in the production of monoclonal antibodies.

Hydrogen bond A non-covalent bond that takes place between an electron deficient hydrogen and an electron rich atom, particularly oxygen and nitrogen.

Hydrogen bond acceptor A functional group that provides the electron rich atom required to interact with a hydrogen in a hydrogen bond.

Hydrogen bond donor A functional group that provides the hydrogen required for a hydrogen bond.

Hydrolases Enzymes that catalyse hydrolysis reactions.

Hydrophilic Refers to compounds that are polar and water soluble. Literally means water loving.

Hydrophobic Refers to compounds that are non-polar and water insoluble. Literally means water hating.

Hydrophobic interactions Refers to the stabilization that is gained when two hydrophobic regions of a molecule or molecules interact and shed the ordered water 'coat' surrounding them. The water molecules concerned become less ordered resulting in an increase in entropy.

Hyperchem A molecular modelling softwear package.

Hypoglycaemia Lowered glucose levels in the blood.

IC_{50} The concentration of an inhibitor required to inhibit an enzyme by 50%.

IND *see* Investigational Exemption to a New Drug Application.

Immunomodulators Agents that either suppress or enhance the immune system.

Immunosuppressants Drugs that inhibit the immune response. Useful in the treatment of autoimmune disease and in reducing the chances of rejection following organ transplants.

Impurity profiling The study of drug batches to identify and quantify any impurities that might be present.

Indicator variables A variable used in QSAR equations which is given the value of one or zero depending on whether a substituent is present or not.

Induced dipole interactions The situation where a charge or a dipole on one molecule induces a dipole in another molecule to allow an ion–dipole interaction or a dipole–dipole interaction respectively. An induced dipole normally requires the presence of π electrons.

Induced fit The alteration in shape that arises in a macromolecule such as a receptor or an enzyme when a ligand binds to its binding site.

Inhibitor An agent that binds to an enzyme and inhibits its activity.

In silico Refers to procedures that are carried out on a computer.

Institutional review board (IRB) A regulatory body in the USA that grants approval to clinical trials at a particular site.

Integrins Molecules displayed on the cells of new blood vessels to protect them from apoptosis.

Investigational Exemption to a New Drug Application A document required by the FDA before clinical trials can begin on a drug.

Iontophoresis A means of encouraging topical absorption of a drug by applying a painless pulse of electricity to increase skin permeability.

Integrase A viral enzyme present in HIV that catalyses the insertion of viral DNA into host DNA.

Integrins Molecules that are involved in anchoring cells to the extracellular matrix.

Intercalating agents Agents containing a planar moiety that is capable of slipping between the base pairs of DNA. Important anticancer and antibacterial agents.

Interferons Endogenous proteins that are part of the body's defence system against viral infections. They work by inhibiting the metabolism of infected cells.

Interleukin-6 A protein that stimulates metastasis

Intermolecular bonds Bonding interactions that take place between two separate molecules.

International preliminary examination report (IPER) A report on a patent application that can be used when applying for patents to individual countries.

International search report (ISR) A report on a patent application that can be used when applying for patents to individual countries.

Intramolecular bonds Bonding interactions other than covalent bonds that take place within the same molecule.

Intramuscular injection The administration of a drug by injection into muscle.

Intraperitoneal injection The administration of a drug by injection into the abdominal cavity.

Intrathecal injection The administration of a drug by injection into the spinal column.

Intravenous injection The administration of a drug by injection into a vein.

Inverse agonist A compound that acts as an antagonist, but which also decreases the 'resting' activity of target receptors (i.e. those receptors that are active in the absence of agonist).

***In vitro* assays, studies or tests** Refers to testing procedures carried out on isolated macromolecules, whole cells or tissue samples.

***In vivo* assays, studies or tests** Refers to studies carried out on animals or humans.

Ion channels Protein complexes in the cell membrane which allow the passage of specific ions across the cell membrane.

Ion channel disrupters A term used to describe a group of antiviral agents that act against the flu virus by disrupting ion channels.

Ion–dipole interactions A non-covalent bonding interaction that takes place between a charged atom and a dipole moment, such as the interaction of a positive charge with the negative end of the dipole.

Ionic interaction A non-covalent bonding interaction between two molecular regions having opposite charges.

Ionophores Agents that act on a cell membrane to produce an uncontrollable passage of ions across the membrane.

Irreversible inhibitor An enzyme inhibitor that binds so strongly to the enzyme that it cannot be displaced.

IsisDraw A chemical drawing softwear package.

Isomerases Enzymes that catalyse isomerizations and intramolecular group transfers.

Isostere A chemical group that can be considered to be equivalent in physical and chemical properties to another chemical group.

Isozymes A series of enzymes that catalyse the same chemical reaction but which differ in their amino acid composition.

K_d The dissociation binding constant.

K_i The inhibitory or affinity constant.

Kinases Enzymes which catalyse the phosphorylation of alcoholic or phenolic groups present in a substrate. The substrate is normally a protein.

Koshland's theory of induced fit *see* induced fit.

Lactamases Bacterial enzymes that hydrolyse the β-lactam ring of penicillins and cephalosporins.

LD_{50} The mean lethal dose of a drug required to kill 50% of the test sample.

Lead compound A compound showing a desired pharmacological property which can be used to initiate a medicinal chemistry project.

LHRH *see* Luteinizing hormone-releasing hormone.

Ligand A term used for any molecule capable of binding to a binding site.

Ligand-gated ion channels Ion channels that are under the control of a chemical messenger or ligand.

Ligases Enzymes that join two substrates together at the expense of ATP hydrolysis.

Lincosamides A group of antibiotics acting against protein synthesis.

Lineweaver–Burk plots Plots which can be used to determine whether an enzyme inhibitor is competitive or non-competitive.

Linker A term used in combinatorial chemistry for a molecule that is covalently linked to a solid phase support and contains a functional group to which another molecule can be attached for the start of a synthesis.

Lipinski's rule of five A set of rules that are obeyed by the majority of orally active drugs. The rules take into account the molecular weight, number of hydrogen bonding groups and the hydrophobic character of the drug.

Lipophilic Refers to compounds that are fatty and non-polar in character. Literally means fat loving.

Liposomes Small vesicles consisting of a phospholipid bilayer membrane. Used to encapsulate drugs for drug delivery.

Local energy minimum Refers to the nearest stable conformation reached when energy minimization is carried out on a molecule by molecular modelling software.

Lock and key hypothesis The now redundant theory that a ligand fits its binding site like a key fitting a lock.

Log P *see* Partition coefficient.

LUDI A software programme used for *de novo* drug design.

LUMO Lowest unoccupied molecular orbital.

Luteinizing hormone-releasing hormone Hormones that are used in anticancer therapy.

Lyases Enzymes that catalyse the addition or removal of groups to form double bonds.

Lysis The process where a cell loses its contents due to weakening of a cell wall or cell membrane.

Lysosomes Membrane-bound structures within eukaryotic cells that contain destructive enzymes.

MAA *see* Marketing authorisation application.

Macrolides Macrocyclic structures that act as antibacterial agents. Erythromycin is the most used example of this class of agents.

Macromolecule A molecule of high molecular weight such as a protein, carbohydrate, lipid or nucleic acid.

Magic bullet *see* Principle of chemotherapy.

Marketing authorization application (MAA) A document provided to the EMEA in order to receive marketing approval for a new drug.

Malignant cancers or tumours Life-threatening tumours that are undergoing metastasis and setting up secondary tumours elsewhere in the body.

Matrix metalloproteinases Enzymes that catalyse the hydrolysis of the proteins making up basement membranes. A target for new anticancer drugs called matrix metalloproteinase inhibitors.

MDRTB Multidrug resistant tuberculosis.

Merrifield resin A resin used in solid phase peptide synthesis.

Messenger RNA (mRNA) Carries the genetic code required for the synthesis of a specific protein.

Me too drugs Drugs which have been modelled as variations of an existing drug.

Metabolic blockers Groups added to a drug to block metabolism at a particular part of the skeleton.

Metalloproteinases Enzymes that catalyse the hydrolysis of peptide bonds in protein substrates and which contain a metal ion as a cofactor in the active site.

Metastasis Refers to the breaking away of individual cancer cells from an established tumour such that they enter the blood supply and start up new tumours elsewhere in the body.

Methylene shuffle A strategy used to alter the hydrophobicity of a molecule. One alkyl chain is shortened by one carbon unit, while another is lengthened by a one carbon unit.

Michaelis constant The Michaelis constant equals the substrate concentration when the reaction rate of an enzyme catalysed reaction is half of its maximum value.

Microfluidics The manipulation of tiny volumes of liquids in a confined space.

Microspheres Small spheres made up of a biologically degradable polymer. Used in drug delivery.

Microtubules Small tubules that are formed in cells by the polymerization of a structural protein called tubulin. Important for cell division and as targets for anticancer drugs.

Mitochondria Organelles within eukaryotic cells that can be viewed as the cell's energy generators. They also play a role in cell apoptosis.

Mitosis The process of cell division.

Mix and split The procedure involved when synthesizing mixtures of compounds by combinatorial synthesis.

Modulator An agent that binds to the allosteric binding site of a target and modulates the activity of that target.

Molar refractivity (*MR*) A measure of a substituent's steric influence in a QSAR equation.

Molecular dynamics A molecular mechanics program that mimics the movement of atoms within a molecule.

Monoamine oxidase inhibitors Compounds that inhibit the metabolic enzyme monoamine oxidase. Have been used as antidepressants but are less favoured now since they have side effects.

Monoclonal antibodies Refers to antibodies that are cloned and are identical in nature.

Monosaccharides The carbohydrate or sugar monomers that make up a polysaccharide.

Motor nerves Nerves carrying messages from the central nervous system to the periphery.

MR *see* molar refractivity.

MRSA Stands for methicillin resistant *Staphylococcus aureus*. Strains of *S. aureus* that have acquired resistance to the penicillin, methicillin.

Multidrug resistance Refers to the situation where a cancer cell acquires resistance to a range of drugs other than the one it was exposed to. Related to the overexpression of P-glycoprotein which expels drugs from the cell.

Murine antibodies Refers to monoclonal antibodies that were originally isolated from mice.

Mutation An alteration in the nucleic acid base sequence making up a gene. Results in a different amino acid in the resultant protein.

Muscarinic receptors One of the two main types of cholinergic receptor.

Mutagen A chemical or substance that induces a mutation in DNA.

NCE *see* New chemical entity.

NDA *see* New drug application.

Neighbouring group participation A mechanism by which a functional group in a molecule assists a reaction without being altered itself.

Nanotubes Tubular structures on the molecular scale which are being considered as possible antibacterial agents.

Neoplasm The proper term for a cancer or tumour. Means new growth.

Nephrons Tubes that collect water and small molecules from the glomeruli and carry these towards the bladder. Much of the water, along with hydrophobic molecules, is reabsorbed into the blood supply from the nephrons and does not reach the bladder.

Neuraminidase An enzyme present in the flu virus that catalyses the hydrolysis of a sialic acid molecule from host glycoconjugates and which is crucial to the infection process.

Neuropeptides Peptides that act as neurotransmitters.

Neurotransmission The process by which neurons communicate with other cells.

Neurotransmitter A chemical released by a neuron ending that acts as a chemical messenger by interacting with a receptor on a target cell.

New chemical entity (NCE) A novel drug structure.

New drug application A document provided to the FDA in order to receive marketing approval for a new drug.

New molecular entity *see* New chemical entity.

Nicotinic receptors One of the two main types of cholinergic receptor.

Nitrogen mustards Alkylating agents used in anticancer therapy.

NME *see* New molecular entity.

NNRTI *see* Non-nucleoside reverse transcriptase inhibitors.

Non-nucleoside reverse transcriptase inhibitors A group of antiviral agents that target an allosteric binding site on the viral enzyme reverse transcriptase.

NRTI *see* Nucleoside reverse transcriptase inhibitors.

Nuclear hormone or transcription receptors *see* Transcription factors.

Nucleases Enzymes that hydrolyse oligonucleotides and nucleic acids.

Nucleic acids RNA or DNA macromolecules made up of nucleotide units. Each nucleotide is made up of a nucleic acid base, sugar and phosphate group.

Nucleocapsid Consists of a viral capsid and its nucleic acid contents. Viral enzymes may be present.

Nucleoside A building block for RNA or DNA that consists of a nucleic acid base linked to a sugar molecule.

Nucleoside reverse transcriptase inhibitors A group of antiviral agents that mimic nucleosides and target the viral enzyme reverse transcriptase.

Nucleosomes Repeating units of histone proteins within a chromatin structure.

Nucleotide A molecule consisting of a nucleoside linked to one, two or three phosphate groups.

NVOC Short hand for the nitroveratryloxycarbonyl protecting group.

Oestrogens Female hormones that are used in anticancer therapy.

Oligonucleotides A series of nucleotides linked together by phosphate bonds. Smaller versions of nucleic acid.

Olivanic acids A group of agents which inhibit beta-lactamases.

Oncogenes Genes which normally code for proteins involved in the control of cell growth and division, but which have undergone a mutation such that they code for rogue proteins, resulting in the uncontrolled growth and division of cells.

Opportunistic pathogens Pathogens which are normally harmless but which cause serious infection when the immune system is weakened.

Organelles Identifiable structures within the cytoplasm of a eukaryotic cell.

Oripavines Complex multicyclic analogues of morphine which have powerful analgesic and sedative properties.

Organophosphates Agents that inhibit the acetylcholinesterase enzyme and which are used as nerve gases, medicines and insecticides.

Orphan drugs Drugs that are effective against rare diseases. Special financial incentives are given to pharmaceutical industries to develop such drugs.

Orphan receptors Novel receptors for which the endogenous ligand is unknown.

Oxazolidinones A group of synthetic antibacterial agents that act against protein synthesis.

Oxidases Enzymes that catalyse oxidation reactions.

Oximinocephalosporins A group of second and third generation cephalosporins.

P1 or P1' Nomenclature used to label the substituents of a substrate that can fit into the binding subsites of an enzyme. P1, P2, P3 etc refers to substituents on one side of the reaction centre, while P1′, P2′, P3′ etc refer to substituents on the other side.

p53 Protein An important protein that monitors the health of the cell and the integrity of its DNA. Important to the apoptosis process.

Papillomavirus A DNA virus responsible for genital warts.

Parasympathetic nerves Nerves of the autonomic motor nervous system that use acetylcholine as neurotransmitter.

Parietal cells Cells lining the stomach which release hydrochloric acid into the stomach.

Partial agonist A drug which acts like an antagonist by blocking an agonist, but which retains some agonist activity of itself.

Partition coefficient (*P*) A measure of a drug's hydrophobic character—usually quoted as a log*P* value.

Patent cooperation treaty (PCT) A treaty to which about 122 countries have signed up to.

PEGylation Covalently linking molecules of polyethylene glycol to macromolecules.

Penicillins Natural and semi-synthetic antibacterial agents that are bactericidal in nature.

Peptidases Enzymes which hydrolyse peptide bonds.

Peptidomimetics Agents that have been developed from peptide lead compounds such that their peptide nature is removed or disguised in order to improve their pharmacokinetic properties.

Peptoids Peptides which are partly or wholly made up of non-naturally occurring amino acids. As such, they may no longer be recognized as peptides by the body's protease enzymes.

P-glycoprotein A protein that expels toxins and drugs from cells. Plays an important role in drug resistance in the anticancer field when cancer cells mutate and produce increased levels of the protein.

Phage *see* Bacteriophage.

Pharmacodynamics The study of how ligands interact with their target binding site.

Pharmacokinetics The study of drug absorption, drug distribution, drug metabolism and drug excretion.

Pharmacophore Defines the atoms and functional groups required for a specific pharmacological activity, and their relative positions in space.

Pharmacophore triangle A triangle connecting three of the important binding centres making up the overall pharmacophore of a molecule.

Partial charges A measure of the partial charge on each atom of a molecule calculated by molecular modelling software.

Partial least squares A statistical method of reaching a QSAR equation in 3D QSAR.

PDGF Platelet-derived growth factor.

Penicillanic acid sulfone derivatives A group of agents which inhibit beta-lactamases.

Penicillinases *see* Lactamases.

Phase I metabolism Reactions undergone by a drug which normally result in the introduction or unmasking of a polar functional group. Most phase I reactions are oxidations.

Phase II metabolism Conjugation reactions where a polar molecule is attached to a functional group that has often been introduced by a phase I reaction.

Phosphatase An enzyme that catalyses the hydrolysis of phosphate bonds.

Phosphodiesterases Enzymes which are responsible for hydrolysing the secondary messengers, cyclic AMP and cyclic GMP.

Phosphorylase An enzyme that catalyses the hydrolysis of phosphate bonds.

Photodynamic therapy The use of light to activate a prodrug in the body—used in cancer therapy.

Photolithography A method of combinatorial synthesis involving the synthesis of products on a solid surface. Reactions only occur on those areas of the surface where photolabile protecting groups have been removed by exposure to light.

Pi (π) bond A weak covalent bond resulting from the 'side on' overlap of p-orbitals. Only occurs when the atoms concerned are sp or sp^2 hybridized, and when the bond between the atoms is a double bond or a triple bond.

Pi (π) bond cooperativity A situation which can arise in conjugated systems where a hydrogen bond donor and a hydrogen bond acceptor enhance their respective hydrogen bonding strengths by a resonance mechanism involving pi bonds.

Picornaviruses A family of viruses that include polio, hepatitis A, cold viruses and foot and mouth viruses.

Pinocytosis A method by which molecules can enter cells without passing through cell membranes. The molecule is 'engulfed' by the cell membrane and taken into the cell in a membrane bound vesicle.

pK_a A measure of the acid/base strength for a drug or a functional group.

pK_i The log of the inhibitory or affinity constant K_i.

Placebo and placebo effect A preparation that contains no active drug, but should look and taste as similar as possible to the preparation of the actual drug. Used to test for the placebo effect where patients improve because they believe they have been given a useful drug, regardless of whether they received it or not.

Placental barrier Membranes that separate a mother's blood from the blood of her foetus. Some drugs can pass through the placental barrier.

Plasma proteins Proteins in the plasma of the blood. Drugs that bind to plasma proteins are unavailable to reach their target.

Plasmid Segments of circular DNA that are transferred naturally between bacterial cells. Useful in cloning and genetic engineering.

Podophyllotoxins A group of natural and semi-synthetic agents used as anticancer agents.

Polymerases Enzymes that catalyse the polymerization of molecular units to form macromolecules.

Polysaccharides Macromolecules consisting of carbohydrate (sugar) monomers.

Porins Protein structures that create pores in the outer membrane of Gram-negative bacteria through which essential nutrients can pass. Some drugs can pass through these pores if they have the correct physical properties.

Potency Refers to the amount of drug required to achieve a defined biological effect.

PRB A powerful growth-inhibitory molecule that binds to a transcription factor to inactivate it

Presynaptic control systems Receptors on the ends of presynaptic neurons that affect the release of neurotransmitter from the neuron.

Principle of chemotherapy The principle where a drug shows selective toxicity towards a target cell but not a normal cell.

Privileged scaffolds Scaffolds that are commonly present in established drugs.

Procaspase 9 An enzyme that activates caspase enzymes to produce apoptosis

Prodrug A molecule that is inactive in itself, but which is converted to the active drug in the body, normally by an enzymatic reaction. Used to avoid problems related to the pharmacokinetics of the active drug and for targeting.

Progestins Hormones that are used in anticancer therapy.

Prokaryotic cells Simple bacterial cells that contain no organelles or well defined nucleus.

Prostaglandins Endogenous chemicals that play an important role as chemical messengers.

Prosthetic group A cofactor which is covalently linked to the active site of an enzyme.

Prostaglandins Natural chemical messengers in the body with a large variety of biological functions.

Protease inhibitors A group of antiviral agents which inhibit the HIV protease enzyme.

Proteases Enzymes which hydrolyse peptide bonds

Protein A macromolecule made up of amino acid monomers. Includes enzymes, receptors, carrier proteins, ion channels, hormones and structural proteins.

Protein kinases *see* Kinases.

Proteoglycan A molecule consisting of a protein and a carbohydrate.

Protomers The protein subunits that make up a viral capsid.

Proteomics A study of the structure and function of novel proteins discovered from genomic studies.

Proto-oncogenes Genes which code for proteins involved in the control of cell growth and division, but which can cause cancer if they undergo mutation to form oncogenes.

Proton pump inhibitors A series of drugs which inhibit the proton pump responsible for releasing hydrochloric acid into the stomach.

q^2 *see* Cross-validated correlation coefficient.

Quantitative structure–activity relationships (QSAR) Studies which relate the physicochemical properties of compounds with their pharmacological activity.

Quinolones A group of synthetic antibacterial agents, largely replaced by fluoroquinolones.

R A symbol used in QSAR equations to represent the electronic influence of a substituent due to resonance effects.

Racemate or racemic mixture A mixture of the various stereoisomers of a molecule. A molecule having one asymmetric centre would be present as both possible enantiomers.

Racemization A reaction which affects the absolute configuration of asymmetric centres to produce a racemic mixture.

Radioligand labelling The use of a radioactively labelled irreversible inhibitor to label a macromolecular target.

Ras protein A small G-protein that plays an important role in the signal transduction pathways leading to cell growth and division.

Receptor A protein with which a chemical messenger or drug can interact to produce a biological response.

Receptor mediated endocytosis Refers to the process by which a virus binds to a host cell glycoprotein and induces endocytosis to enter the cell.

Recombinant DNA technology The process by which DNA is manipulated to produce new DNA. Involves the controlled splitting of DNA from different sources, followed by the formation or recombination of hybrid DNA.

Recursive deconvolution A method of identifying the constituents in a combinatorial synthetic mixture. The method requires the storage of intermediate mixtures.

Reductases Enzymes that catalyse reduction reactions.

Regression coefficient A measure of how well a QSAR equation explains the variance in biological activity of a series of drugs.

Relaxation time The time taken for excited nuclei to return to their resting state in NMR spectroscopy.

Renal Refers to the kidney.

Replication The process by which DNA produces a copy of itself.

Restriction enzymes Enzymes that are used in recombinant DNA technology to split DNA chains in a controlled fashion.

Reverse transcriptase A viral enzyme present in HIV that catalyses DNA from an RNA template.

Reverse transcriptase inhibitors A group of antiviral compounds that inhibit the viral enzyme reverse transcriptase.

Reversible inhibitors Enzyme inhibitors that compete with the substrate for the enzyme's active site and which can be displaced by increasing the concentration of substrate.

Ribosomes Structures consisting of ribosomal RNA and protein which bind messenger RNA and catalyse the synthesis of the protein coded by mRNA.

Ribosomal RNA (rRNA) Present in ribosomes as the major structural and catalytic component.

Ribozymes RNA molecules with an enzymatic property.

Rifamycins A group of antibiotics and semi-synthetic agents used as antibacterial agents.

Rigidification strategies Strategies used to limit the number of conformations that a drug can adopt with the aim of retaining the active conformation.

Ring contraction/expansion strategy The variation of ring size in a drug to optimise the relative positions of different binding groups.

Ring fusion or extension strategy The fusion of one ring onto another to enhance a drug's binding interactions.

Ring variation strategies The replacement of an aromatic, heteroaromatic or saturated ring with a different ring system to obtain different structural classes of a drug.

Rink resin A resin used in combinatorial chemistry.

RNA Ribonucleic acid.

RNA-dependent RNA polymerase An enzyme that catalyses the synthesis of RNA from an RNA template.

RNA viruses Viruses that contain RNA as their nucleic acid.

S1 or S1′ Nomenclature use to label binding subsites of an enzyme. The subsites accept the amino acid residues of a peptide substrate. S1, S2, S3 etc refers to subsites on one side of the reaction centre, while S1′, S2′, S3′ refer to subsites on the other side.

Safety catch linker An example of a linker in combinatorial chemistry on which two molecules can be constructed, one the target molecule and the other a tagging molecule.

SAR *see* Structure–activity relationships.

Sarcodictyins Naturally occurring anticancer agents that inhibit tubulin depolymerization.

SARS Severe acute respiratory syndrome. A viral infection.

Scaffolds Refers to the molecular core of a drug onto which the important binding groups are attached as substituents.

Scatchard plot A plot used to measure the affinity of a drug for its binding site.

Schild analysis Used to determine the dissociation constant of competitive antagonists.

Screening A procedure by which compounds are tested for biological activity.

Scintillation proximate assay A visual method of detecting whether a ligand binds to a target by its ability to compete with a radiolabelled ligand that emits light in the presence of scintillant.

Secondary messenger A secondary messenger is a natural chemical which is produced by the cell as a result of receptor activation, and which carries the chemical message from the cell membrane to the cytoplasm.

Secondary metabolites Natural products that are not crucial to cell growth and division. Generally produced in mature cells.

Self-assembly The process by which molecular units assemble into a structure without the aid of enzymes or other structures; for example the assembly of protomers to form a viral capsid.

Self-destruct drugs Drugs which are designed to be inactivated in the body through chemical or enzymatic mechanisms.

Semi-synthetic product A product that has been synthesized from a naturally occurring compound.

Sensitization The process by which a cell adapts to the continued presence of an antagonist, resulting in increased receptor sensitivity or the production of more receptors.

Sequential blocking Describes the situation where two agents inhibit two different enzymes in a biosynthetic pathway. Allows each agent to be administered in lower and safer doses.

Sequential release Refers to the sequential release of the products of a combinatorial synthesis from the solid support.

Serine-threonine kinases Enzymes which catalyse the phosphorylation of serine and threonine residues in protein substrates.

Sigma (σ) bond A strong covalent bond taking place between two atoms. It involves strong overlap between two atomic orbitals whose lobes point towards each other.

Signal transduction The mechanism by which an activated receptor transmits a message into the cell, resulting in a cellular response.

Simplification strategies The simplification of a drug to remove functional groups, asymmetric centres and skeletal frameworks that are not required for activity.

Small G-proteins Proteins that have an important role in signal transduction pathways. So called because they are similar to G-proteins but are a single protein.

Small nuclear RNA Small molecules of RNA that are in the nucleus and are a constituent of a spliceosome. They are important to the modification and splicing of messenger RNA following transcription.

'Smart' drugs Anticholinesterases that act in the central nervous system to increase levels of acetylcholine. They relieve the symptoms of Alzheimer's disease.

Soft drugs Refers to drugs that are designed to undergo metabolism in a predictable manner to produce non-toxic, inactive metabolites that are excreted.

Somatic gene therapy The use of a carrier virus to smuggle a gene into a human cell that has a defective form of the gene.

Somatic motor nervous system Motor nerves carrying messages to skeletal muscle.

Specifications Refer to the tests that have to be carried out on a manufactured drug, and the standards of purity required.

Spider scaffolds Scaffolds which have binding group substituents placed round the whole scaffold.

Spindle Refers to the arrangement of microtubules that is formed in order to separate cells during cell division.

Spliceosome A structure made up of protein and small nuclear RNA. Serves to modify and splice mRNA following transcription.

***ss*DNA** Single-stranded DNA. A term used in virology.

***ss*RNA** Single-stranded RNA. A term used in virology.

Steady-state concentration The concentration of a drug that is maintained in the blood supply following regular administrations.

Stereoelectronic modifications The addition or alteration of groups to protect labile functional groups by steric and electronic means.

Steric shields Groups that are added to molecules to protect vulnerable groups by nature of their size.

Streptogramins A group of macrocyclic antibiotics acting against protein synthesis.

Structure–activity relationships Studies carried out to determine those atoms or functional groups which are important to a drug's activity.

Structure-based drug design The design of drugs based on a study of their target binding interactions with the aid of X-ray crystallography and molecular modelling.

Subcutaneous injection The administration of a drug by injection under the surface of the skin.

Subsites Often refers to enzymes that accept peptides or proteins as substrates. The subsites are binding pockets that accept amino acid residues from the substrate.

Substituent hydrophobicity constant (π) A measure of a substituent's hydrophobic character.

Substrate A chemical which undergoes a reaction that is catalysed by an enzyme.

Suicide substrates Enzyme inhibitors which have been designed to be activated by an enzyme catalysed reaction, and which will bind irreversibly to the active site as a result.

Sulfonamides Synthetic antibacterial drugs that are bacteriostatic in nature.

Supercoiling The process by which DNA coils into a compact shape.

Suppositories Drug preparations that are administered rectally.

Sulfotransferases Enzymes that catalyse conjugation reactions involving sulfate groups.

Surface plasmon resonance An optical method of detecting the binding of a ligand with its target.

Sybyl A molecular modelling softwear package.

Sympathetic nerves Nerves of the autonomic motor nervous system that use noradrenaline as a neurotransmitter at target cells and which use acetylcholine as a neurotransmitter between neurons.

Synapse The small gap between a neuron and a target cell, across which a neurotransmitter has to travel in order to reach its receptor.

Synergy An effect where the presence of one drug enhances the activity of another.

Tadpole scaffold A scaffold where substituents acting as binding groups are located at one region of the scaffold.

Taft's steric factor (E_s) A measure of a substituents steric influence in QSAR equations.

Tagging A method of identifying what structures are being synthesised on a resin bead during a combinatorial synthesis. The tag is a peptide or nucleotide sequence which is constructed in parallel with the synthesis.

Tautomers The different structures that a conjugated system can adopt arising from the rearrangement of double bonds and hydrogen atoms.

Taxoids Naturally occurring and semi-synthetic anticancer agents that inhibit tubulin depolymerization.

Telomerase An enzyme that catalyses the construction of telomeres.

Telomeres Polynucleotide structures at the 3′ ends of chromosomes that stabilise DNA.

Tetracyclines Tetracyclic antibiotics that are bacteriostatic in their action.

Teratogen A compound that produces abnormalities in a developing foetus.

TGF Transforming growth factor.

Therapeutic index or ratio The therapeutic index is the ratio of a drug's undesirable effects with respect to its desirable effects and is therefore a measure of how safe that drug is. Usually this involves comparing the dose levels leading to a toxic effect with respect to the dose levels leading to a therapeutic effect. The larger the therapeutic index, the safer the drug.

To be more precise, the therapeutic index compares the drug dose levels which lead to toxic effects in 50% of cases studied, with respect to the dose levels leading to maximum therapeutic effects in 50% of cases studied. This is a more reliable method of measuring the index since it eliminates any peculiar individual results.

Therapeutic window The range of a drug's plasma concentration between its therapeutic level and its toxic level.

Thymidylate synthase Catalyses the synthesis of an important building block for DNA. Inhibitors are used as anticancer agents.

Thrombospondin An endogenous compound that inhibits angiogenesis.

TNF and TNF-R Tumour necrosis factors and tumour necrosis factor receptors. Play a role in apoptosis or cell death.

Transdermal absorption Refers to the absorption of a drug through the skin.

Tolerance Repeat doses of a drug may result in smaller biological results. The drug may block or antagonise its own action and larger doses are needed for the same pharmacological effect. Alternatively, the body may 'learn' how to metabolize the drug more efficiently. Again, larger doses are needed for the same pharmacological effect, increasing the chances of toxic side effects.

Topliss scheme A scheme used to determine which substituents should be introduced in order to get more active drugs—useful when analogues are synthesized and tested one at a time.

Topoisomerases Enzymes that catalyse transient breaks in one or both strands of DNA to allow coiling and uncoiling of the molecule. These act as targets for several antibacterial and anticancer drugs.

Transcription The process by which a segment of DNA is copied to messenger RNA.

Transcription factors Complexes which bind to DNA and control the expression of specific genes.

Transduction The process by which plasmids are exchanged between bacterial cells.

Transfer RNA (tRNA) An RNA molecule that bears an amino acid which is specific for a particular triplet of nucleic acid bases.

Transferases Enzymes that catalyse transfer reactions.

Transgenic animals Animals that have been genetically modified such that they can be used for the *in vivo* testing of drugs.

Translation The process by which proteins are synthesized based on the genetic code present in mRNA.

Transition state A high energy intermediate that must be formed during an enzyme-catalysed reaction. The energy required to reach the transition state determines the rate of reaction. It is proposed that an enzyme binds the transition state more strongly than the substrate or the product resulting in a stabilization of the transition state.

Transition-state analogues or inhibitors Enzyme inhibitors which have been designed to mimic the transition state of an enzyme-catalysed reaction.

Transition-state isostere An arrangement of atoms that mimics the arrangement of atoms in a transition state, but which is more stable.

Transpeptidases Important bacterial enzymes that catalyse the final cross-linking of the bacterial cell wall. Targeted by penicillins and cephalosporins.

Transport proteins *see* Carrier proteins.

Tricyclic antidepressants A series of tricyclic compounds that have antidepressant activity by blocking the uptake of noradrenaline from nerve synapses back into the presynaptic neuron.

Triplet code Refers to the fact that the genetic code is read in sets of three nucleic acid bases at a time. Each triplet codes for a specific amino acid.

Tumour suppression genes *see* Anti-oncogenes.

Tyrosine kinases Enzymes which catalyse the phosphorylation of tyrosine residues in protein substrates.

Ureidopenicillins A group of penicillins bearing a urea group at the α-position.

Vaccination The introduction of foreign antigens to prime the immune system such that it will work more effectively against later infections.

van der Waals interactions Weak interactions that occur between two hydrophobic regions and which involves interactions between transient dipoles. The dipoles arise from uneven electron distributions with time.

Varcella zoster viruses Viruses responsible for chicken pox and shingles.

Vascular endothelial growth factor A growth factor that stimulates angiogenesis.

Vectors Refer to the process by which a molecule can be taken into a cell. Particularly important to gene therapy.

VEGF *see* Vascular endothelial growth factor.

Veins Blood vessels carrying blood back to the heart.

Verloop steric parameter A measure of a substituent's steric properties. Used in QSAR equations.

Vesicle A membrane bound 'bubble' within the cell. Neurotransmitters are stored within vesicles prior to release.

Vinca alkaloids Naturally occurring compounds that inhibit tubulin polymerisation and are used as anticancer agents.

Virion The form that a virus takes when it is not within a host cell.

VIRSA Vancomycin resistant *Staphylococcus aureus*

Viruses Non-cellular infectious agents consisting of DNA or RNA wrapped in a protein coat. Require a host cell to multiply.

Voltage-gated ion channels Ion channels that are controlled by the potential difference across the cell membrane. Important to the mechanism of transmission in neurons.

VRE Vancomycin resistant enterococci.

VZV *see* Varcella zoster viruses.

Wang resin A resin used in combinatorial chemistry.

Withdrawal symptoms The symptoms that arise when a drug associated with physical dependence is no longer taken.

Z A short-hand term for the protecting group, benzyloxycarbonyl.

Zinc finger domains Refers to a region of a steroid receptor that is rich in cysteine residues and zinc cofactors. Involved in binding to DNA when the receptor is part of a transcription factor.

General further reading

It is recommended that you read round various topics as much as you can. There are strengths and weaknesses in every publication and if you find an explanation difficult to follow in one textbook or article, you may find a clearer one in a different publication. Textbooks also differ in the breadth and detail of coverage given to the various topics of medicinal chemistry. For example, this textbook has chapters concentrating in some detail on topics such as antibacterial, antiviral, and anticancer agents, but does not cover cardiovascular or anti-inflammatory agents to the same extent. The following are useful reference and general texts. You will also find references to articles and books at the end of each chapter that are more specific to the topics covered in that chapter.

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