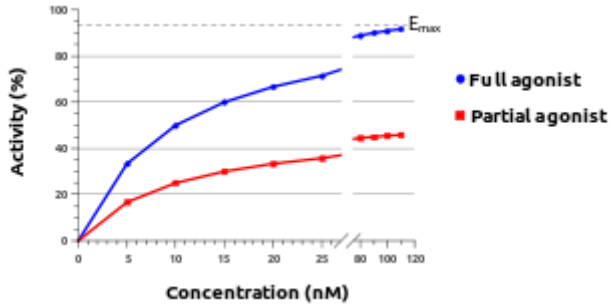
Agonist

An **agonist** is a chemical that binds to a receptor and activates the receptor to produce a biological response. In contrast, an antagonist blocks the action of the agonist, while an inverse agonist causes an action opposite to that of the agonist.



Agonists activating hypothetical receptors.

Contents

Etymology

From the Greek **αγωνιστής** (agōnistēs), contestant; champion; rival < **αγων** (agōn), contest, combat; exertion, struggle < **αγω** (agō), I lead, lead towards, conduct; drive

Types of agonists

Receptors can be activated by either endogenous agonists (such as hormones and neurotransmitters) or exogenous agonists (such as drugs), resulting in a biological response. A physiological agonist is a substance that creates the same bodily responses but does not bind to the same receptor.

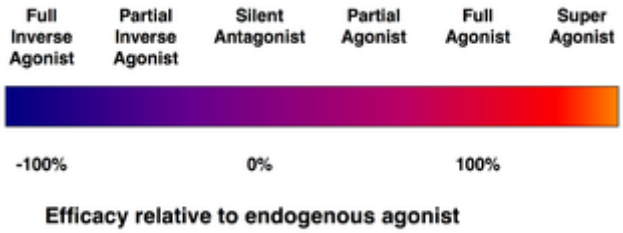
- An endogenous agonist for a particular receptor is a compound naturally produced by the body that binds to and activates that receptor. For example, the endogenous agonist for serotonin receptors is serotonin, and the endogenous agonist for dopamine receptors is dopamine.[1]
- **Full agonists** bind to and activate a receptor with the maximum response that an agonist can elicit at the receptor. One example of a drug that can act as a full agonist is isoproterenol, which mimics the action of adrenaline at β adrenoreceptors. Another example is morphine, which mimics the actions of endorphins at μ-opioid receptors throughout the central nervous system. However, a drug can act as a full agonist in some tissues and as a partial agonist in other tissues, depending upon the relative numbers of receptors and differences in receptor coupling.
- A **co-agonist** works with other co-agonists to produce the desired effect together. NMDA receptor activation requires the binding of both glutamate, glycine and D-serine co-agonists. Calcium can also act as a co-agonist at the IP3 receptor.
- A **selective agonist** is selective for a specific type of receptor. E.g. buspirone is a selective agonist for serotonin 5-HT1A.

- Partial agonists (such as buspirone, aripiprazole, buprenorphine, or norclozapine) also bind and activate a given receptor, but have only partial efficacy at the receptor relative to a full agonist, even at maximal receptor occupancy. Agents like buprenorphine are used to treat opiate dependence for this reason, as they produce milder effects on the opioid receptor with lower dependence and abuse potential.
- An inverse agonist is an agent that binds to the same receptor binding-site as an agonist for that receptor and inhibits the constitutive activity of the receptor. Inverse agonists exert the opposite pharmacological effect of a receptor agonist, not merely an absence of the agonist effect as seen with an antagonist. An example is the cannabinoid inverse agonist rimonabant.
- A superagonist is a term used by some to identify a compound that is capable of producing a greater response than the endogenous agonist for the target receptor. It might be argued that the endogenous agonist is simply a partial agonist in that tissue.
- An irreversible agonist is a type of agonist that binds permanently to a receptor through the formation of covalent bonds. A few of these have been described, including Paracetamol.[2][3]
- A biased agonist is an agent that binds to a receptor without affecting the same signal transduction pathway. Oliceridine is a μ-opioid receptor agonist that has been described to be functionally selective towards G protein and away from β-arrestin2 pathways.[4]

New findings that broaden the conventional definition of pharmacology demonstrate that ligands can concurrently behave as agonist *and* antagonists at the same receptor, depending on effector pathways or tissue type. Terms that describe this phenomenon are "functional selectivity", "protean agonism",[5][6][7] or selective receptor modulators.[8]

Activity

Potency



Efficacy spectrum of receptor ligands.

Potency is the amount of agonist needed to elicit a desired response. The potency of an agonist is inversely related to its EC_{50} value. The EC_{50} can be measured for a given agonist by determining the concentration of agonist needed to elicit half of the maximum biological response of the agonist. The EC_{50} value is useful for comparing the potency of drugs with similar efficacies producing physiologically similar effects. The smaller the EC_{50} value, the greater the potency of the agonist, the lower the concentration of drug that is required to elicit the maximum biological response.

Therapeutic index

When a drug is used therapeutically, it is important to understand the margin of safety that exists between the dose needed for the desired effect and the dose that produces unwanted and possibly dangerous side-effects (measured by the TD_{50}, the dose that produces toxicity in 50% of individuals). This relationship, termed the therapeutic index, is defined as the ratio TD_{50}:ED_{50}. In general, the narrower this margin, the more likely it is that the drug will produce unwanted effects. The therapeutic index emphasizes the importance of the margin of safety, as distinct from the potency, in determining the usefulness of a drug.

See also

- Allosteric modulator
- Dose response curve
- Excitatory postsynaptic potential
- Functional selectivity
- Intrinsic activity
- Inverse agonist
- Mixed agonist/antagonist
- Receptor antagonist
- Receptor theory

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