Eudysmic ratio

The **eudysmic ratio** (also spelled **eudismic ratio**) represents the difference in pharmacologic activity between the two enantiomers of a drug. In most cases where a chiral compound is biologically active, one enantiomer is more active than the other. The eudysmic ratio is the ratio of activity between the two. A eudysmic ratio significantly differing from 1 means that they are statistically different in activity.

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Terminology

The **eutomer** is the chiral enantiomer having the desired pharmacological activity,[1] e.g., as an active ingredient in a drug.

The **distomer**, on the other hand, is the enantiomer of the eutomer which may have undesired bioactivity or may be bio-inert.[2]

A racemic mixture is an equal mixture of both enantiomers, which may be easier to manufacture than a single enantiomeric form.

It is often the case that only a single one of the enantiomers contains all of the wanted bioactivity, the distomer is often less active, has no desired activity or may even be toxic.[3] In some cases, the eudysmic ratio is so high, that it is desired to separate out the two enantiomers instead of leaving it as a racemic product. It is also possible that the distomer is not simply completely inactive but actually antagonizes the effects of the eutomer. Alternatively, it is possible that the distomer converts in the body into the eutomer, at least partly.

Calculation

One way the eudysmic ratio is computed is by dividing the EC_{50} or the IC_{50} of the eutomer by the same measurement of the distomer.[4][5] Whether one chooses to use the EC_{50} or IC_{50} depends on the drug in question.

Examples

- Citalopram is a case example of such a compound, and steps were taken to separate out the weaker enantiomer.
- Thalidomide is a drug whose two enantiomers cause distinctly different effects from one another. This is an example where the two enantiomers of a drug have *different* pharmacologic

effects.

- Methorphan is another drug whose two enantiomers possess very different binding profiles, with the L enantiomer being a potent opioid analgesic, and the D enantiomer being a commonly used over-the-counter cough suppressant which acts as an NMDA-antagonist but possesses nearly no opioid activity. In the case of morphinan, the eudysmic ratio is preserved after metabolism as the D and L metabolites possess the same pharmacological targets as the corresponding methorphan enantiomers, but are considerably more potent than their parent compounds.
- Amino acids are also a very interesting example of eudysmic ratio. Nearly all of the amino acids in the human body are called "L" amino acids; despite being chiral, the body almost exclusively creates and uses amino acids in this one configuration. D amino acids, the enantiomers - or "mirror images" - of the amino acids in the human body cannot be incorporated into proteins. D-aspartate and D-serine are two notable counterexamples, since they do not appear to ever be incorporated into proteins, but instead act individually as signalling molecules. However, mammals can metabolize significant amount of D amino acids by oxidizing them to alpha-ketoacids (most of which are non-chiral) and then transaminases can create L amino acids. There are no reasons to believe that humans are exceptional, they have all required enzymes (DDO, DAO). Some common foods contain near-racemic mixtures of amino acids.

See also

- Enantiopure drug

References

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