

## ***Stereochemical issues in pharmaceutical synthesis - Selected examples***

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### **I. Challenges and strategies in pharmaceutical synthesis**

#### **1. Drug development process**

- 1.1. From lead discovery to marketed drugs
- 1.2. Extraction, hemi-synthesis, total synthesis

#### **2. Stereochemistry in bioactive molecules**

- 2.1. Chirality, from life to health.
- 2.2. Resolution and enantioselective synthesis
- 2.3. Enantioselective catalysis: academic and industrial research efforts towards *L*-DOPA

#### **3. The chiral switch**

- 3.1. The need for pure eutomers
- 3.2. Example: from ceterizine to levoceterizine

#### **4. The chiral pool**

- 4.1. Natural chiral pool: beyond (*L*)-aminoacids and (*D*)- saccharides, alkaloids & terpenes
- 4.2. Artificial chiral pool

### **II. Selected examples of stereochemical challenges in chiral drug synthesis**

#### **1. Chiral anti-cancer drugs**

- 1.1. Vinorelbine (Navelbine<sup>®</sup>)
- 1.2. Taxol and Taxotere
- 1.3. Bryostatine
- 1.4. Atrasentan

#### **2. Chiral anti-inflammatory drugs**

- 2.1. Corticosteroids
  - The steroid family
  - Cortisone
- 2.2. Arylpropionic acids

#### **3. Chiral anti-microbial drugs**

- 3.1. Anti-bacterial (antibiotics): from beta-lactams to fluoroquinolones
- 3.2. Anti-mycobacterial (tuberculosis): rifampicin, ethambutol
- 3.3. Anti-parasitic (antimalarial): artemisinin
- 3.4. Anti-viral (HIV): AZT, efavirenz

#### **4. Chiral psychotropic drugs**

- 4.1. Neuroleptics = antipsychotics (tranquilizers)
  - phenothiazines: promethazine, levomepromazine, alimemazine and mequitazine
  - benzamides: levosulpiride *vs* *rac*-amisulpride
- 4.2. Anxiolitics = depressants
  - Barbiturates: methohexital
  - Benzodiazepines: oxazepam
- 4.3. Antidepressants
  - propargylic amines: rasagiline, selegiline
  - beta, gamma, delta-aminoalcohols: dapoxetine, fluoxetine (Prozac<sup>®</sup>)

#### **5. Chiral vitamins**

- 5.1. Vitamine C (anti-oxidant): ascorbic acid
- 5.2. Vitamine D (calcitropic): from calciferols to calcitriols

### **III. Conclusions and prospects**