AL Chemistry Group Project

Topic: Metformin

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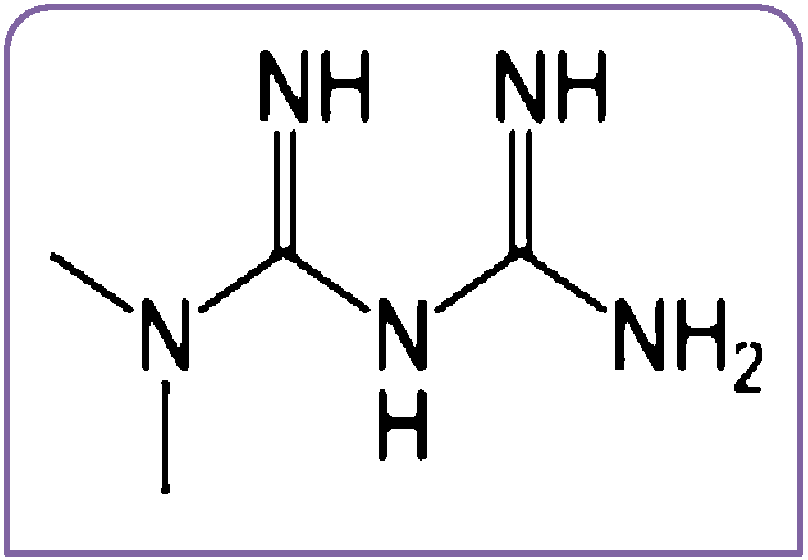
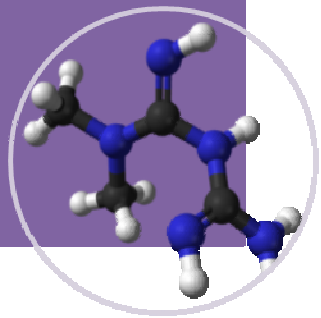
Structural formula of metfomrin



IUPAC name: *N,N*-dimethylimidodicarbonimidic diamide



It can …..

- helps control blood sugar levels
- Treat type 2 diabetes (insulin independent)


Lead compound discovery
Molecular modification
Formulation development
Safety tests and human trials
Approval for marketing

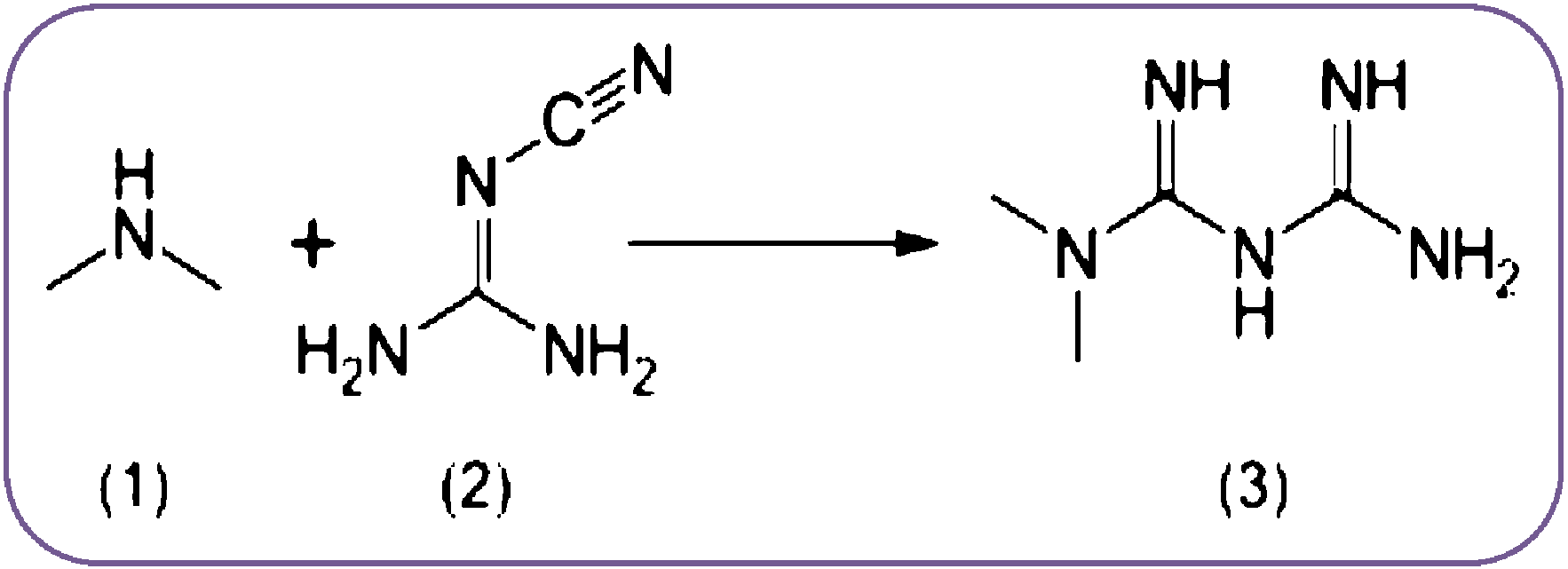
Lead compound discovery

Lead compound

- a plant called French lilac (*Galega officinalis*)
- serves as a prototype

- first described in the scientific literature in 1922, by Emil Werner and James Bell
- product in the synthesis of *N*,*N*-dimethylguanidine
- Jean Sterne re-investigate the blood sugar lowering activity of metformin
- He successfully found out the efficacy of metformin in the treatment of type 2 diabetes on humans in 1957

Molecular modification



(1) dimethylamine hydrochloride
(2) 2-cyanoguanidine

(3)precipitates with 96% yield(metformin hydrochloride)

under the condition of heating

Remarks:

- quimolar amount of(1) and (2) dissolved in toluene
- quimolar amount of hydrogen chloride is slowly added
- after cooling (3) precipitates with 96% yield.

Formulation development

- Metformin IR (immediate release) is available in 500 mg, 850 mg, and 1000 mg tablets

- Metformin SR (slow release) or XR (extended release) was introduced in 2004, in 500 mg and 750 mg

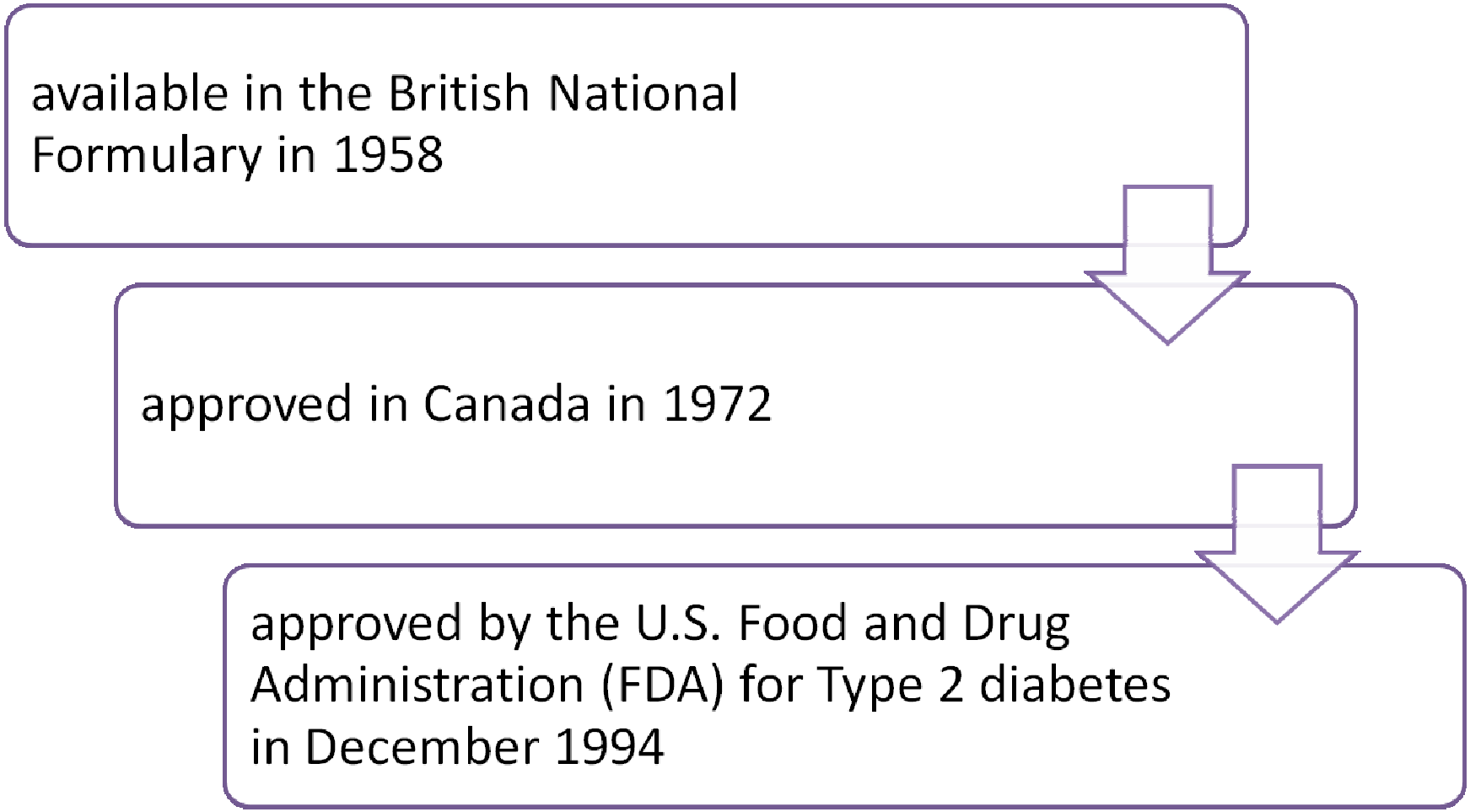
In 2002, metformin is prescribed to type 2 diabetes patients in combination with rosiglitazone

In the United States, metformin is also available in combination with pioglitazone, sulfonylureas glipizid…….

Safety tests and human trials

1929	• scientists Slotta and Tschesche discovered the sugar-lowering action of metformin in rabbits
1950	• physician, Eusebio Y.Garcia believed metformin to have bacteriostatic, antiviral, antimalarial, antipyretic and analgesic actions
1954	• Polish pharmacologist Janusz Supniewski observed same antiviral effects in humans
1957	• French diabetologist Jean Sternewas was the first to try metformin on humans for the treatment of diabetes

Approval for marketing



marketed in the United States, beginning on March 3, 1995

in the United States alone, more than 40 million prescriptions were filled in 2008 for its generic formulations

Now, it is believed to be the most widely prescribed anti-diabetic drug in the world

Reference:

- http://www.medicinenet.com/metformin/article.htm
- http://www.drugs.com/metformin.html
- http://en.wikipedia.org/wiki/Metformin