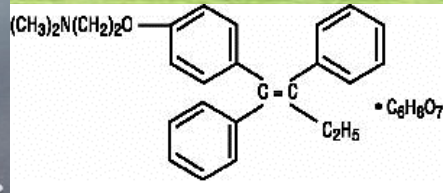
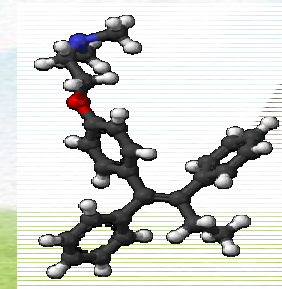
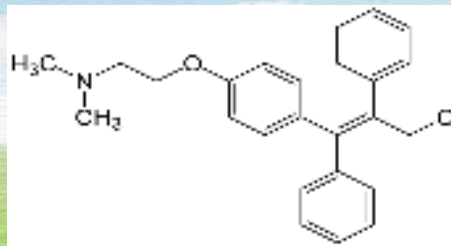


AL Chemistry Group Project (TAS)

Drugs development:

Tamoxifen

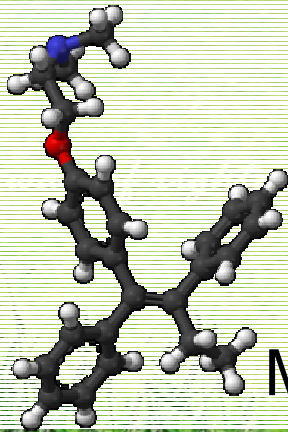


6S Cheng Hoi Wah (5)
6S Tang Chi Chung (21)
6S Wong Chung Ming (26)

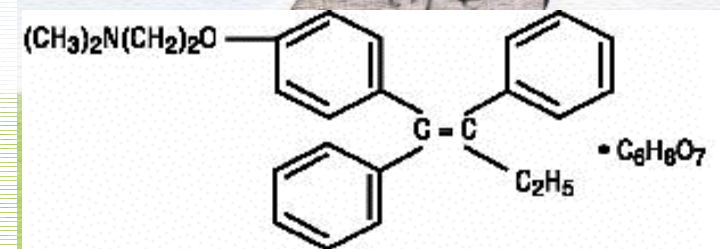
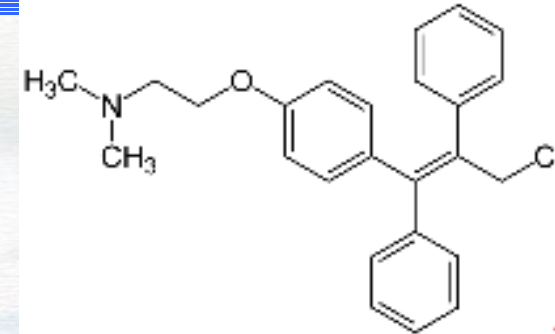


Introduction to Tamoxifen

- Tamoxifen citrate tablets USP
→ **nonsteroidal antiestrogen**
- trans-isomer of a **triphenylethylene** derivative: (Z)-2-[4-(1,2-diphenyl-1-butenyl)phenoxy]-N,N-dimethylethanamine 2-hydroxy-1,2,3-propanetricarboxylate (1:1)



Molecular Weight: 563.62



Lead compound discovery

1950s

Origin:

birth control pill >> nonsteroidal antioestrogens

anticancer drug

1962

>> compound ICI46,474 (focus on birth control)

triphenylethylenes

Tamoxifen

4

Lead compound discovery (2)

1967

Harper & Walpole

trans isomer of a substituted triphenylethylene:

Tamoxifen

- estrogen antagonists



- inhibit the growth of cancer cells 😊

→ breast cancer cells

Lead compound discovery (3)

1970 s

laboratory testing at ICI Pharmaceuticals
estrogen receptor alpha ligand (a protein)
+estrogen
+estrogen diol
=create new cancer cells

Tamoxifen

- inhibit this bonding process
- slow the creation of cancer cells

Molecular modification

1. organic modifications
2. inorganic modifications
3. organometallic modifications

tamoxifen + ferrocene moiety = ferrocifen

Molecular modification (2)

McMurry coupling route:

incorporation of $\text{CpRe}(\text{CO})_3$ into the tamoxifen skeleton



multiple low-valent metal

→ can be oxidized to yield a multiply-charged cluster

→ more effective **TUMOUR SUPPRESSION**

Formulation development

given alone??

→ 😊 combination: chemotherapeutic drugs:
5-fluorouracil (5-FU, or fluorouracil), (5-
fluorouracil, epirubicin, cyclophosphamide)

→ a 42% improvement in disease-free
survival at 9 years compared to tamoxifen
alone

∴ Tamoxifen: potential toxicity

*Treated with **Melatonin**

→ improve the safety and efficacy of tamoxifen

→ fewer side effects in these patients than those receiving tamoxifen alone,

→ significant tumor regression in 4 of the 14 patients receiving melatonin



Tamoxifen

Side effect

Side effect: hot flashes

Paroxetine: antidepressant

GLA + tamoxifen.

Inositol hexaphosphate (IP-6)

>>> increasing the effectiveness of tamoxifen
in blocking breast cancer cell growth.

effective against ER alpha-negative cells
and adriamycin-resistant cell lines.

Clinical trials

- Adverse reactions: relatively mild
- Increased bone and tumor pain,
- local disease flare,
- a good tumor response.
- increased bone pain.
- soft tissue disease,
- sudden increases in the size of preexisting lesions,
- marked erythema within and surrounding the lesions and/or the development of new lesions.
- hot flashes.
- hypercalcemia, peripheral edema, distaste for food, pruritus vulvae, depression, dizziness, lightheadedness, headache, hair thinning and/or partial hair loss, and vaginal dryness.



Reference

- Medicine online
- www.medicineonline.com/drugs/T/2941/TAMOXIFEN-CITRATE-TABLETS-USP.html
- Wikipedia
- <http://en.wikipedia.org/wiki/Tamoxifen>
- PubMed
- <http://www.ncbi.nlm.nih.gov/pubmed/20091826>
- Alternativehealth
- www.alternativehealth.co.nz/cancer/melatonin/chemo.htm
- Anabolics
- www.anabolics.ca/tamoxifen.php
- Druglib
- www.druglib.com/druginfo/nolvadex/side-effects_adverse-reactions
- Drugs.com
- www.drugs.com/sfx/nolvadex-side-effects.html
- Journal of Organo metallic Chemistry
- http://www.enscp.fr/labos/UMR7576/site%20avril%2004/PDF_labopub2006/Chan%28JOMC%292006.pdf

END



In the way of righteousness there is life; along that path is immortality.