MACROCYCLES DERIVED WITH ANTICANCER ACTIVITY

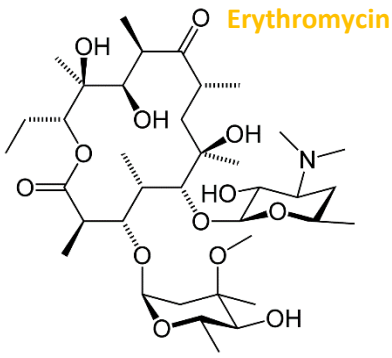
Patent Application: **MX/a/2016/002862**

Status: patent pending

Abstract: This invention describes a novel, easy and economical methodology for synthesizing compounds based on the macrolide skeleton of natural products. These compounds have shown highly selective cytotoxic activity against cancerous cells and could represent a new option in the treatment of cancer with fewer side effects.

Background:

The macrocyclic skeleton is a macrostructure highly common in natural sources. This structure is like the one presented by compounds like the erythromycin, an antibiotic. This chemical composition provides a wide range of biological activities:



antituberculosis, insecticides, antivirals, analgesics, anti-inflammatories, anti-cancer drugs, antihypertensives, antioxidants, antidiabetics.

An example of the impact that these macrostructures have on medicinal chemistry field is the vinblastine, a natural product successfully used as chemotherapeutic agent. Currently, its synthesis is made in a sustainable way through synthetic methodologies without depleting the natural resource.

The structural complexity of these natural compounds has led to the design and development of directed synthesis methods that replicate the macrostructure of similar natural compounds, in a more economic and efficient way, to produce new compounds with pharmacological properties against cancer.

Stage of research:

The method presented in this invention allows to achieve a practical synthesis in few steps of reaction and purification of new macrocycles with cytotoxic activity

Without affect the healthy cells. Additionally, the macrocycles compounds have shown to be useful against the following cancer cell lines:

human colorectal adenocarcinoma, human breast adenocarcinoma, human chronic myelogenous leukemia, human glioblastoma, human prostatic adenocarcinoma, human lung adenocarcinoma.

The results indicate the great potential of these compounds in the biological application in the search of therapies for patients with prostate cancer.

Applications fields

This development is highly important in the chemical, pharmaceutical and medicinal industries, since the design and production of new organic and inorganic structures is an important step in the development of new bioactive molecules suitable for therapeutic use.

The macrocyclic compounds of this invention exhibit properties of interest in the field of cancer chemistry and biology.

Advantages

The present development describes a new methodology for the construction of unpublished macrocycles, inspired by the macrocycle skeleton of natural products, obtained through easy and economically viable synthetic methods

The obtained **products**:

- ✓ Present properties of interest in the cancer chemistry and biology field
- ✓ Allowed to develop a library of compounds synthesized in a targeted manner (possible drugs with cytotoxic activity).
- ✓ Presented selective cytotoxic activity.
- ✓ Could be useful in the cancer therapy.

Some macrocyclic compounds have a cytotoxic activity comparable to the cisplatin's. This result is very valuable, since it is known that cisplatin is a highly used anticancer, but also highly toxic and poorly selective towards a particular cell line.

The macrocycles of the present invention did not exhibit cytotoxicity in healthy cells, allowing them to

be candidates for the generation of anticancer drugs with less or even no side effects.

Additionally, the **method** has also good advantages:

- ✓ Combining various reaction steps in few steps.
- ✓ Simpler purification procedures.
- ✓ More environmentally friendly process.

These features make this method faster and more economic, which could be very convenient.

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