

5-Fluorocytosine

Nucleobase analog for *in vitro* and *in vivo* cytotoxicity assays

Catalog # sud-5fc

For research use only

Version # 12C14-MM

PRODUCT INFORMATION

Content:

5-Fluorocytosine (5-FC) is supplied as one bottle of a colorless, water soluble solution at a concentration of 10 mg/ml, filtered to sterility for customer convenience.

- sud-5fc: 250 mg at 10 mg/ml

Shipping and Storage:

5-FC is shipped at room temperature. Store at room temperature in a cool and dark place.

5-FC is stable for one year when properly stored.

SPECIAL HANDLING

Caution should be exercised during the handling and disposal of this product due to potential toxic, mutagenic and carcinogenic properties. Wear gloves when handling this drug. See Materials Safety Data Sheet (MSDS) for safe handling.

GENERAL PRODUCT USE

5-Fluorocytosine is a fluorinated analog of cytosine. 5-FC is approved by the U.S. Food and Drug Administration (FDA) as an antifungal agent used for the treatment of *Candida* and *Cryptococcus*. With the development of gene therapy, 5-FC has been introduced as a prodrug in combination with the cytosine deaminase suicide gene.

BACKGROUND

Mammalian cells are resistant to therapeutic concentrations of 5-fluorocytosine due to their lack of cytosine deaminase (CD), an enzyme only found in prokaryotes and lower eukaryotes. CD converts 5-FC into 5-fluorouracil (5-FU), a highly cytotoxic compound routinely used in cancer chemotherapy. 5-FC is used in combination with the *E. coli* CD gene (*codA*) or *S. cerevisiae* CD gene (*fcy*) in suicide gene therapy protocols. To increase the cytotoxicity of 5-FC and therefore reduce the concentration of the prodrug administered, InvivoGen has designed *E. coli codA::upp* and *S. cerevisiae fcy::fur* fusion genes (for more details visit our website www.invivogen.com).

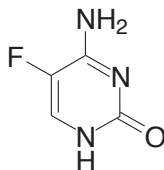
CHEMICAL PROPERTIES

CAS number: 2022-85-7

Formula: C₄H₄FN₃O

Molecular weight: 129.1

Structure::



MECHANISM OF ACTION

5-Fluorocytosine is deaminated to 5-fluorouracil by cytosine deaminase, an enzyme from the pyrimidine salvage pathway. The cytotoxicity of 5-FU is largely exerted following its conversion, by a two-step route, to 5-fluoro-uridine monophosphate (5-FUMP). 5-FUMP is further transformed to 5-fluoro-deoxyuridine monophosphate (5-FdUMP), an irreversible inhibitor of thymidylate synthase and hence of DNA synthesis by deprivation of deoxythymidine triphosphate (dTTP) (Fig. 1).

5-FU can also follow another enzymatic pathway where it is primarily degraded to nontoxic β-alanine. To circumvent this catabolic pathway by orientating 5-FU towards the formation of 5-FUMP, InvivoGen has engineered fusions between *E. coli* or *S. cerevisiae* cytosine deaminase and uracil phosphoribosyltransferase (UPRT) genes. In prokaryotes and lower eukaryotes, UPRT catalyzes the direct conversion of 5-FU to 5-FUMP, whereas in mammalian cells which lack this enzyme, 5-FU is converted to 5-FUMP through the concerted action of two highly regulated enzymes. Expression of CD::UPRT fusions has been demonstrated to increase 5-FC cytotoxicity in cell culture as well as *in vivo*.

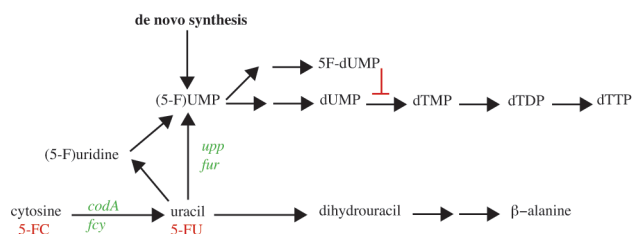


Figure 1: Metabolism of 5-FC. Abbreviations are: *upp*, *E. coli* uracil phosphoribosyl-transferase; *fur*, *S. cerevisiae* uracil phosphoribosyltransferase; *codA*, *E. coli* cytosine deaminase; *fcy*, *S. cerevisiae* cytosine deaminase.

METHOD

Cytotoxicity assay

- 1- Seed cells at a density of 1×10^3 cells/well in a 96-well microtiter plate containing 100 μ l of culture medium.
- 2- Prepare a set of sterile stock dilutions of the 10 mg/ml solution provided.
- 3- One day later, add increasing concentrations of 5-FC to the wells.
Note: Remember to include a control well without the prodrug.
- 4- After 5-7 days, wash cells with fresh medium and assess cytotoxicity by trypan blue exclusion using a hemocytometer to quantify the results.

TECHNICAL SUPPORT

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