Chemsketch Study of 5-Fluorouracil (5FU) : A chemotherapy drug

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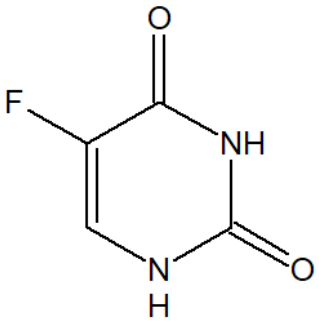
Abstract: 5-fluorouracil (5-FU) is an antimetabolite drug that is widely used for the treatment of cancer particularly for colorectal cancer. Anticancer activity of 5-FU can be increased by understanding the mechanism of action of 5-FU. Properties of 5-Fluorouracil (5FU) are studied theoretically by employing web tool of ACD chemsketch.

Keywords: 5-Fluorouracil, ACD/ChemSketch, ACD/3D Viewer

Introduction

An anticancer medication 5-Fluorouracil(5FU) interferes with DNA synthesis and gradually slows growth of these cancer cells and further kills them[1-5]. (Fig 1). 5-FU is used in some ophthalmological and dermatological conditions. It is used to treat actinic keratosis[6] (pre-cancerous skin lesions) and basal cell carcinoma and it works by selectively destroying sun-damaged skin cells. 5-FU is also used in ophthalmology[7] for conditions like glaucoma filtering, dacryocystorhinostomy, pterygium, and vitreoretinal surgery. 5-FU is available in various forms, including creams for topical application and injections for systemic treatment



5-fluoropyrimidine-2,4(1*H*,3*H*)-dione

Figure 1. structure of 5-Flurouracil

Hypothetical Study of 5-Flurouracil Using Chemsketch Software

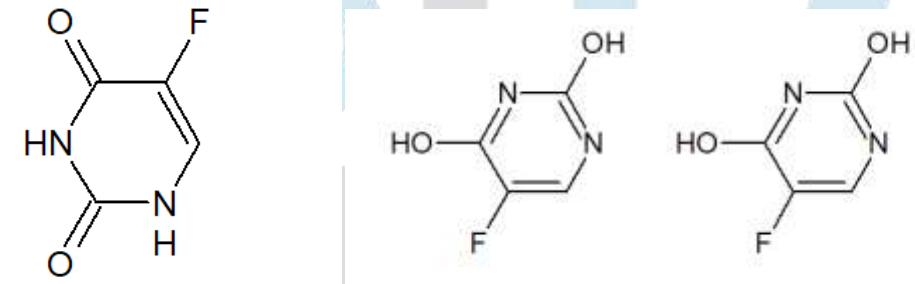
ACD/Labs software provides a Chemical Naming Service which is used to name compounds quickly and accurately. Systematic names according to IUPAC and CAS Index nomenclature rules can be generated by employing ACD. A variety of molecular descriptors can be calculated by the application of ACD/ChemSketch[8-10]. As determined by Chemsketch the molecular formula of 5Flurouracil is $C_4H_3FN_2O_2$ and and its Molecular Weight is 130.0772232. IUPAC name of 5-Flurouracil is 5-fluoro-1H-pyrimidine-2,4-dione[11].

The structure of chemical species can be described by simplified molecular-input line-entry system (SMILES)[12] which is in form of a line notation. SMILES strings are further imported by molecule editors and are converted into two-dimensional drawings or three-dimensional models of the molecules. Smiles notation of 5Flurouracil is FC1=CNC(=O)NC1=O (Table.1) and the structure of 5FU drawn from SMILES is given in figure 2.

An input chemical structure (in the form of a 'connectiontable') is converted to a unique and predictable set of ASCII characters so that InChI label is generated. Under IUPAC project during the period 2000–2004 InChI procedures were developed[13]. At the US National Institute of Standards and Technology (NIST) the technical development was carried out. InChI name of 5-flurouracil is 1S/2C4H3FN2O2/c2*5-2-1-6-4(9)7-3(2)8/h2*1H,(H2,6,7,8,9). InChI . Structure of 5-flurouracil is displayed in figure 2. GHASVSINZRGABV-UHFFFAOYSA-N represents the InChI key of 5-flurouracil.

Table.1 Chemical naming of 5-flurouracil as determined by ACD/chemsketch

IUPAC name	**5-fluoro-1H-pyrimidine-2,4-dione**
InChI name	**1S/2C4H3FN2O2/c2*5-2-1-6-4(9)7-3(2)8/h2*1H,(H2,6,7,8,9)**
SMILES notation	**FC1=CNC(=O)NC1=O**
InChI Key	GHASVSINZRGABV-UHFFFAOYSA-N



(i) **(ii)**

Figure 2. Structure of 5-flurouracil from (i) SMILES and (ii) from InChI

The most favorable tautomeric form is the drawn chemical structure. Selected structure does not have Markush fragments and does not have Stereoisomers.

Properties of 5-flurouracil as determined by ACD/chemsketch

Properties for compounds like prediction of Molecular formula, Formula weight, Composition, Molar refractivity, Molar volume, Parachor, Index of refraction, Surface tension, Density, Dielectric constant, Polarizability, Monoisotopic, nominal, and average mass are predicted by ACD/ ChemSketch.

Table 2. Properties of 5-flurouracil as determined by acd/chemsketch

Molecular Formula:	**$C_4H_3FN_2O_2$**
Formula Weight:	**130.0772232**
Composition:	**C(36.93%) H(2.32%) F(14.61%) N(21.54%) O(24.60%)**
Molar Refractivity:	**25.85 ± 0.4 cm^3**
Molar Volume:	**84.5 ± 5.0 cm^3**
Parachor:	**220.4 ± 6.0 cm^3**

Index of Refraction:	**1.523 ± 0.03**
Surface Tension:	**46.1 ± 5.0 dyne/cm**
Density:	**1.53 ± 0.1 g/cm^3**
Dielectric Constant:	**Not available**
Polarizability:	**10.24 ± 0.5 10^{-24}cm^3**
RDBE:	**4**
Monoisotopic Mass:	**130.017856 Da**
Nominal Mass:	**130 Da**
Average Mass:	**130.0772 Da**
M+:	**130.017307 Da**
M-:	**130.018404 Da**
[M+H]+:	**131.025132 Da**
[M+H]-:	**131.026229 Da**
[M-H]+:	**129.009482 Da**
[M-H]-:	**129.010579 Da**

log P of 5-flurouracil

The propensity of a neutral molecule to differentially dissolve in two immiscible phases is measured in terms of a quantitative descriptor of lipophilicity Partition constant P. logarithmic ratio (log*P*) from structure which is an estimate of the value of the octanol-water partitioning coefficient is provided by log*P* prediction model. ACD/Log*P* is used worldwide by chemists in various arms of chemical research. Calculated log P of 5-flurouracil is -0.78+/- 0.31.

3D Viewer –3D Optimised Forms of 5-flurouracil

An accurate 3D modeling and visualization program ACD/3D Viewer [14,15] is fully integrated with ACD/ChemSketch. It is employed to draw 2D structures and thereby allows to obtain their 3D representations in color display.ACD/3D Viewer is a powerful program that presents various styles of structure 3D representation. 3D structure can be displayed in various forms like wireframe, wireframe model with labels, Ball and stick model, stick model ,dots forms, Dots only, discs only, Spacefill, discs Spacefill with dots, Wireframe with dots, Sticks with dots, Ball and stick with dots and Disks as displayed in figures 4,5

ACD/3D Viewer is employed to

i. Manipulate 3D models
ii. Display a 3D structure
iii. Add an overlay of small-dots and is used to Measure and change bond lengths, bond angles
iv. move, 2D and 3D rotate, also at a fixed angle, resize, change styles, and colors
v. Display a 3D structure as stick, ball-and-stick, spheres, or disks
vi. Optimize the structure using a 3D CHARMM-type of force field
vii. Switch from 3D to 2D display in the ChemSketch window at the click of a button
viii. Set the 3D structure to Auto-rotate, with or without changing the style of structure display
ix. Rotate and move selected atoms rather than entire structures
x. Change and delete atoms, assign the center of rotation to an atom
xi. View 3D structure in perspective
xii. Export 3D models to other geometry optimization programs

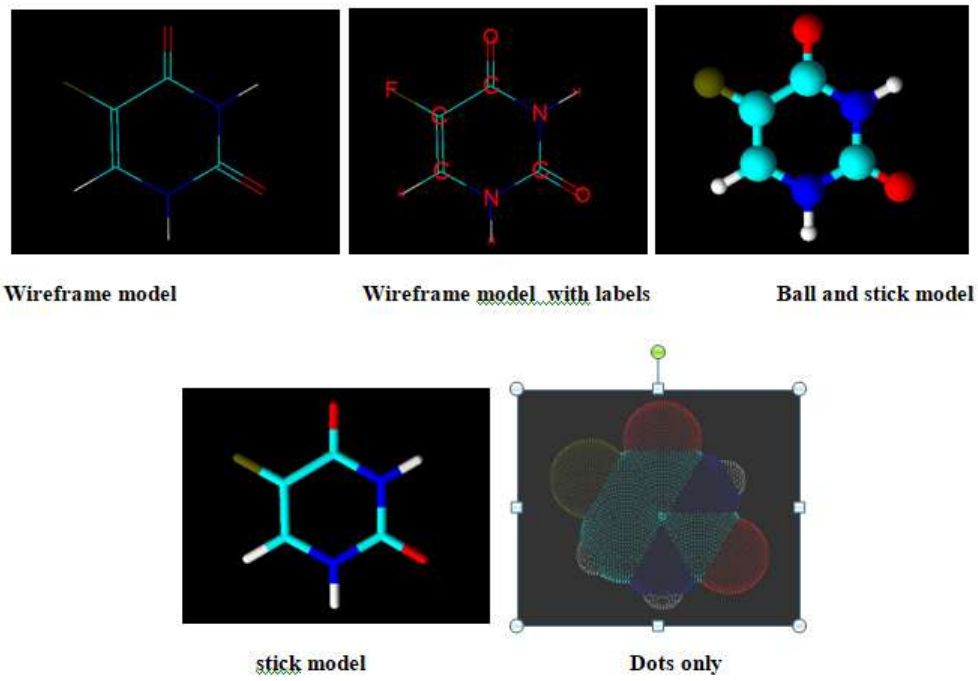


Figure 4. 3D optimized wireframe, Wireframe model with labels, Ball and stick model, stick model ,dots forms of 5-flurouracil

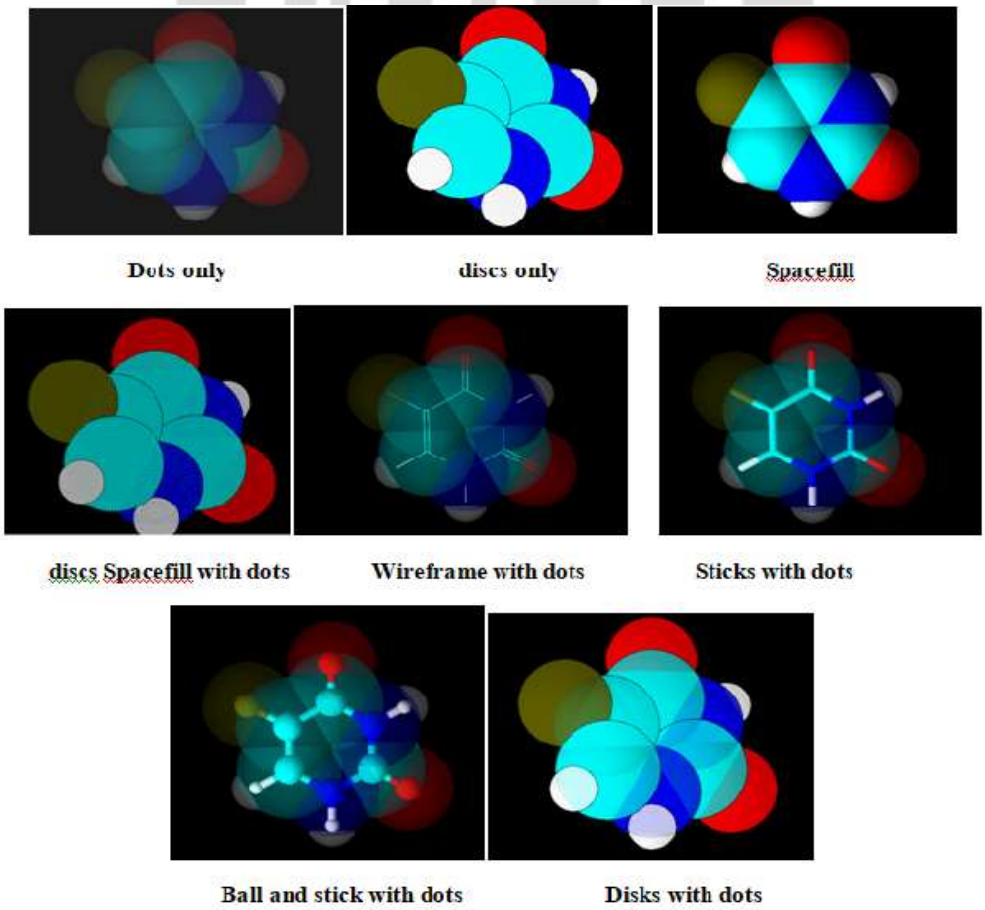


Figure 5. 3D optimized Dots only, discs only, Spacefill, discs Spacefill with dots, Wireframe with dots, Sticks with dots, Ball and stick with dots and Disks with dots of 5-flurouracil

Conclusion

From the above computational studies, it is clearly inferred that 5-flurouracil is a chemically reactive compound. Physicochemical aspects of 5FU were clearly interpreted by the Chemsketch study. The presence of potential donor atoms in 5FU were confirmed by the calculation of physicochemical properties. These studies present us the opportunity to take a critical look at this novel compound.

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