Molecular Menagerie

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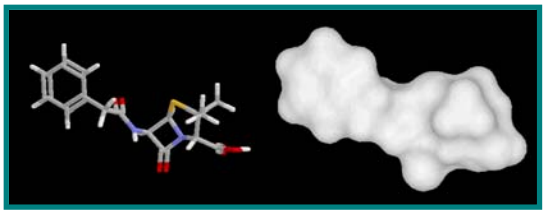
What are models for?

Scientists often use molecular models to study how the functions of chemically and biologically important molecules relate to molecular structure and to the overall shape and size of the molecules.

Recent advances in 3-D graphics have made the use of computer models much easier. Working with 3-D models now requires only a regular desktop PC, not a supercomputer (see penicillin G models above). Nevertheless, physical models still remain useful for teaching and demonstrations.



Penicillin G molecule: Stick and 3-D surface models.

On the following pages, you will find chemical formulas and 3-D structural diagrams of some interesting natural and artificial molecules that you can build with a kit.

To build some models, you will have to team up with one or more colleagues.

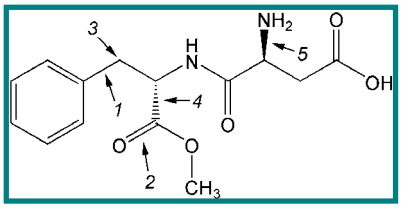
Suggested Molecular Model Kits

This activity was designed for a molecular model kit containing:

14 Carbon (C; black)
2 Nitrogen (N; blue)
8 Oxygen (O; red)
10 Chloride (Cl; green)
1 Sulfur (S; yellow)
20 Hydrogen (H; white)
10 Flexible bonds (white)
40 Covalent bonds (green)

Any kit would do, but one possibility is a combination of Hubbard's Organic Chemistry Molecular Model Kit (RG-84-0220 in Carolina Biological Supply Catalog; 12 pack) and Hubbard's Molecular Models Kit (RG-94-0222; 12 pack).

How to Read a Chemical Formula



If you are not too familiar with the notations in a chemical formula, here's a quick review (see annotated diagram).

1. Single covalent bonds between atoms are denoted by a single line. You will use the green stiff bonds in your kit for these.
2. Double covalent bonds between atoms are denoted by a double line. You will use the white flexible bonds in your kit to represent these.
3. In these formulas, carbon atoms are usually omitted from the diagram, along with hydrogen atoms that are bonded to them. For example, at point 3 in the diagram, there is a carbon atom with two attached hydrogen atoms (CH_2).
4. Three-dimensional information is sometimes shown with wedges. A dashed wedge denotes a bond going away from the viewer into the plane of the page at the broad end of the wedge.
5. A solid wedge denotes a bond coming toward the viewer out of the plane of the page at the broad end of the wedge.

What Are You Eating?

Do you ever wonder what kind of molecule caffeine is? How about Nutrasweet? Here are some examples of chemicals in common refreshments and sweeteners.

Coffee (caffeine)

Table sugar (sucrose)

Fruit juice (glucose)

Fruit juice (fructose)

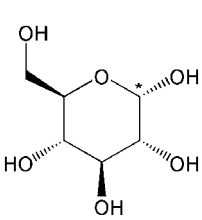
Nutrasweet artificial sweetener (aspartame)

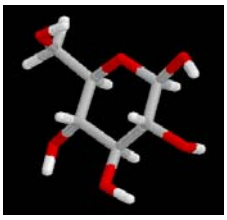
Milk (lactose)

Chocolate (serotonin)

Sweet 'n Low artificial sweetener (saccharin)

Glucose ($C_6H_{12}O_6$): Fruit Juice





Glucose is a 6-membered sugar that is found in honey and many fruit juices. It is also the main sugar in the blood.

Glucose can occur in two different 3-D forms (see sidebar).

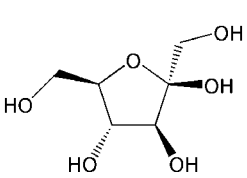
Requires one kit

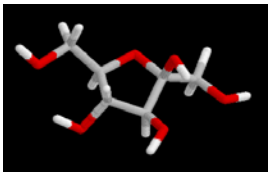
Glucose can differ in how the -OH group on the carbon atom (denoted by an asterisk) is attached.

The formula diagram shows α-D-glucopyranose. α indicates that the -OH group is below the plane of the ring. The 3-D view shows β-D-glucopyranose. β indicates that the -OH group is above the plane.

In two-ringed sugars,such as sucrose and lactose, the various combinations of different α sugars and β sugars can become rather complex.

Fructose ($C_6H_{12}O_6$): Fruit Juice

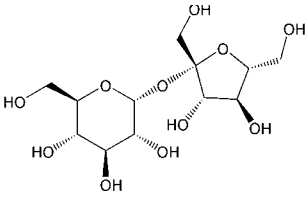


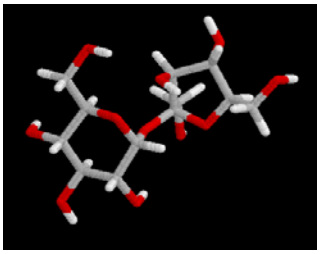


Fructose is a 5-membered sugar. Refined from corn starch, it is thought to be sweeter than sucrose, particularly when cold or in solution. It therefore is a good candidate for a low-calorie sweetener. Unfortunately, it tends to be converted to fat rather than glycogen.

Requires one kit

Sucrose ($C_{12}H_{22}O_{11}$): Sugar

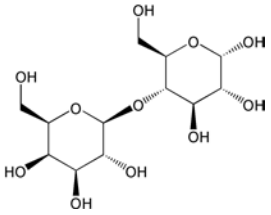


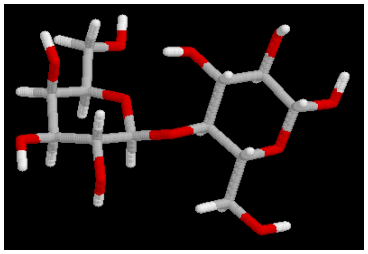


Sucrose is a two-ringed sugar containing a glucose joined to a fructose. Refined from sugarcane or beets, it is available as common table sugar.

Requires two kits

Lactose ($C_{12}H_{22}O_{11}$): Milk

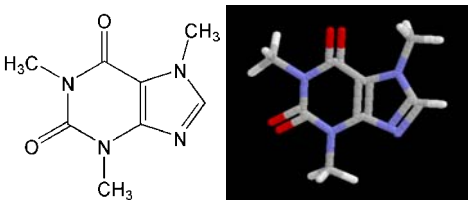




Lactose consists of a glucose joined to a galactose (galactose is very similar to glucose, differing only in the 3-D position of one –OH group). It is contained in milk.

Requires two kits

Caffeine ($C_8H_{10}N_4O_2$): Coffee

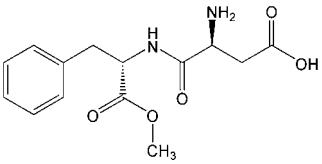


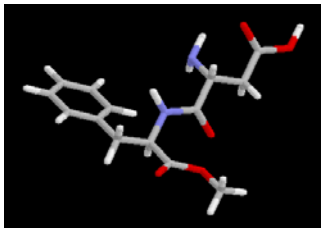
Caffeine is a cardiac stimulant and a diuretic.

In the nervous system, it binds to an adenosine receptor but does not activate it. This binding action interferes with the sleep response and also causes secretion of adrenaline.

Requires two kits

Aspartame ($C_{14}H_{18}N_2O_5$): Nutrasweet

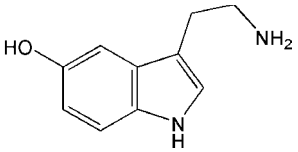


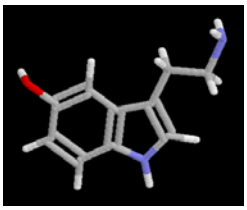


Aspartame, popularly known by its trade name Nutrasweet, is an artificial sweetener that is thought to be 200 times sweeter than sugar.

Requires two kits

Serotonin ($C_{10}H_{12}N_2O$): Chocolate

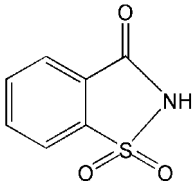


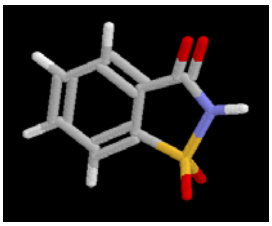


Chocolate contains a variety of chemical compounds, such as phenylethylamine, theobromine, caffeine, and serotonin. Serotonin is a brain neurotransmitter.

Requires one kit

Saccharin ($C_7H_5NO_3S$): Sweet 'n Low





Saccharin is an artificial sweetener that is thought to be 500 times sweeter than sugar.

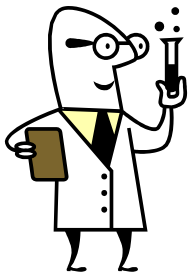
Requires one kit

Simulating Diversity-Oriented Synthesis (DOS)

When you build a molecular model by looking at a formula, you are doing a kind of directed synthesis.

If instead you build molecules by randomly selecting parts, that's almost like diversity-oriented synthesis.

In reality, there are many chemical constraints that limit what kind of molecules can be built, but you can imagine that the end result may be a huge number of possibly novel molecules.



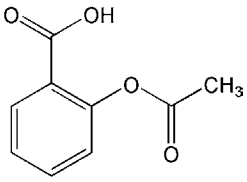
Molecules you can build with one kit

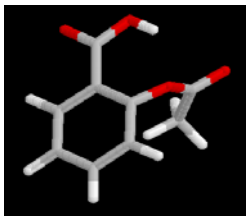
Aspirin and ibuprofen have analgesic (painkilling), antipyretic (fever-reducing), and anti-inflammatory properties. Acetaminophen is an analgesic and antipyretic.

The analgesic and anti-inflammatory action is mediated by inhibition of prostaglandin synthesis. Prostaglandins carry and intensify pain signals and induce inflammation.

The antipyretic effect results from the drugs' action in the hypothalamus, which causes increased peripheral blood flow and thus leads to faster heat dissipation.

Aspirin ($C_9H_8O_4$)

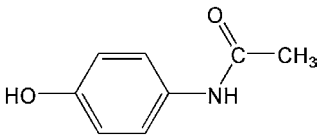


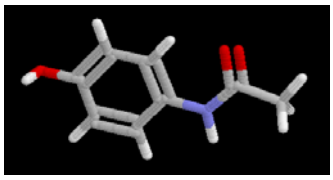


Aspirin, one of the first drugs to become widely available, is an analgesic, anti-inflammatory, antipyretic (fever-reducing) drug.

It binds to the active site of cycloxygenase and blocks the synthesis of prostaglandins, key hormones that are produced by cells to carry and intensify pain signals and induce inflammation.

Acetaminophen ($C_8H_9NO_2$)

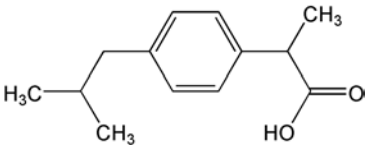


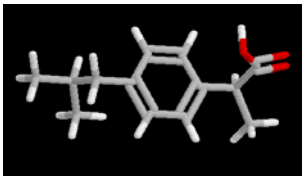


Acetaminophen (active ingredient in Tylenol) is an analgesic and an antipyretic.

The analgesic effect is achieved by inhibiting prostaglandin synthesis in the brain but not in the periphery (thus it doesn't have anti-inflammatory effects).

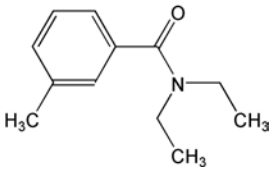
Ibuprofen ($C_{13}H_{18}O_2$)

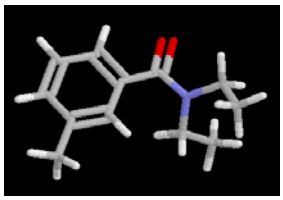




Ibuprofen is an anti-inflammatory agent with analgesic and antipyretic effects.

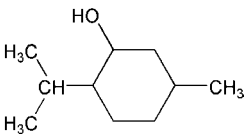
DEET ($C_{12}H_{17}NO$)

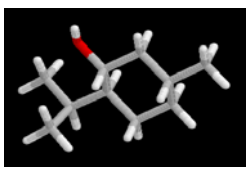




DEET (N, N-diethyl-3-methyl benzamide) is the most commonly used insect repellent in the United States.

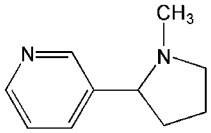
Menthol ($C_{10}H_{20}O$)

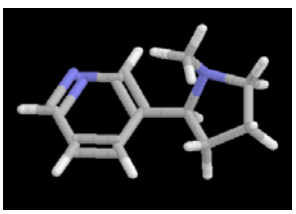




Menthol is a naturally occurring substance in the oils of the mint tree. Its uses include menthol cigarettes, over-the-counter rubs, and mouthwashes.

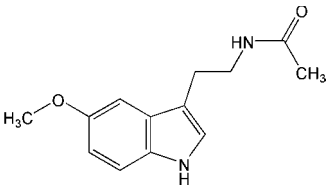
Nicotine ($C_{10}H_{14}N_2$)

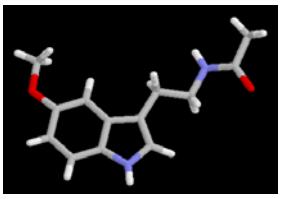




Nicotine is the addictive agent in tobacco. In purified form, nicotine has also been used as an insecticide.

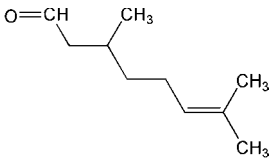
Melatonin ($C_{13}H_{16}N_2O_2$)

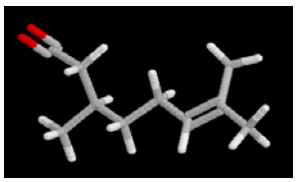




Melatonin is a hormone that is involved in the regulation of circadian, or daily, internal rhythm.

Citronellal ($C_{10}H_{18}O$)

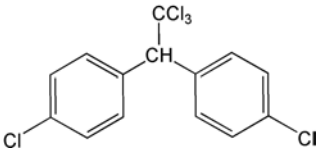


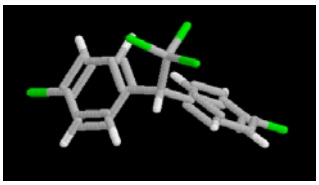


Citronellal is extracted from oils of the citronella plant. It is used as a natural insect repellent.

Molecules you can build with two kits

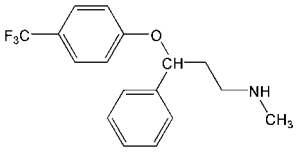
DDT ($C_{14}H_9Cl_5$)

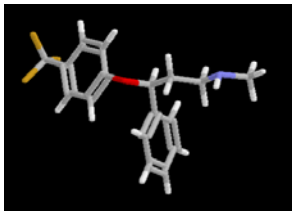




DDT (dichloro-diphenyl-trichloroethane) was once used widely as an insecticide. Its use was banned in the United States in 1973. It is highly toxic to fish and causes various problems in other animals.

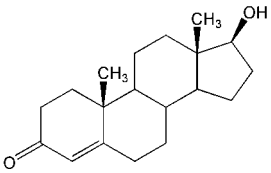
Prozac ($C_{17}H_{18}F_3NO$)

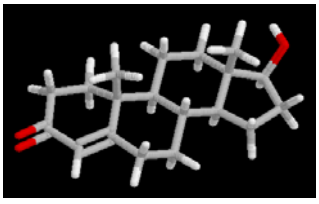




Prozac is the trade name for fluoxetine hydrochloride, the world's most widely prescribed antidepressant.

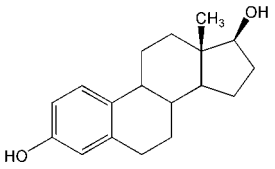
Testosterone ($C_{19}H_{28}O_2$)

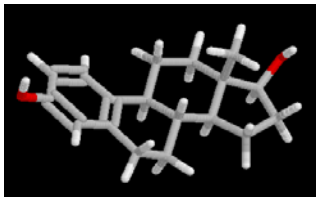




Tesosterone is a natural steroid hormone. It is responsible for the development of male secondary sex characteristics.

Estradiol ($C_{18}H_{24}O_2$)

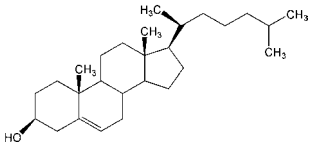




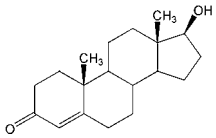
Estradiol is an estrogen, a steroid hormone required for the development of female secondary sex characteristics.

Both testosterone and estradiol are synthesized from cholesterol in a series of steps.

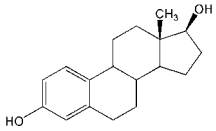
In the following diagrams, you can see that the core ring structures are similar in these molecules.



Cholesterol



Testosterone

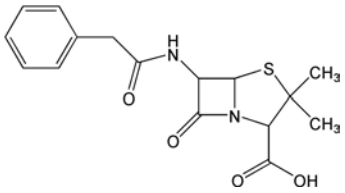


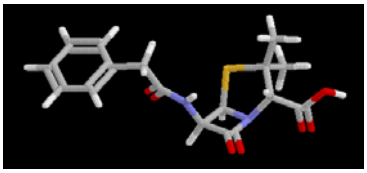
Estradiol

The penicillin family of antibiotics works by preventing the proper formation of the bacterial cell wall. The affected bacteria fail to divide, and they grow abnormally long. Eventually, they are unable to resist the osmotic pressure and rupture.

Cholesterol, a lipid and therefore hydrophobic, isn't found free-floating in the bloodstream. Instead, protein packages known as lipoproteins form a shell around cholesterol to shield it from the aqueous environment. HDL (high-density lipoprotein) cholesterol and LDL (low-density lipoprotein) cholesterol are two types of cholesterol complexes that are well known for their involvement in atherosclerosis and heart attacks.

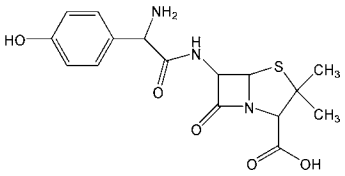
Penicillin G ($C_{16}H_{18}N_2O_4S$)

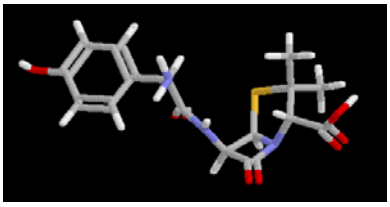




Also known as benzyl penicillin. Penicillin is not a single compound but a group of closely related compounds. All contain the same basic ringed structure.

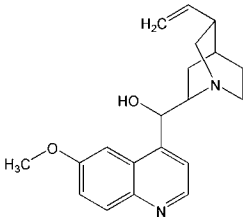
Amoxicillin ($C_{16}H_{19}N_3O_5S$)

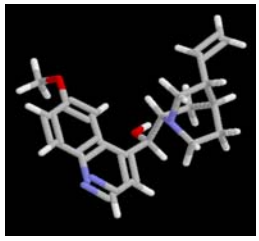




Amoxicillin is another member of the penicillin family of antibiotics.

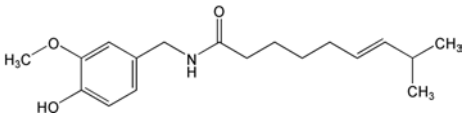
Quinine ($C_{20}H_{24}N_2O_2$)

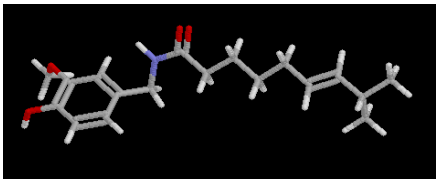




Quinine is an antimalarial drug that was first isolated from the bark of the cinchona tree of South America.

Capsaicin ($C_{18}H_{27}NO_3$)

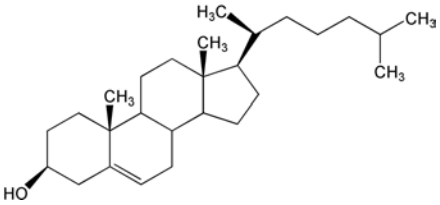


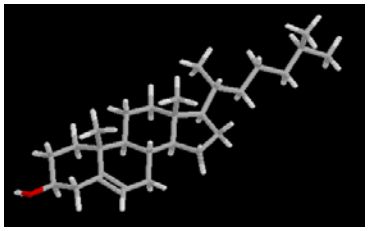


Capsaicin is the substance that makes various peppers taste hot. It is also used as an animal and insect repellent.

Molecules you can build with three kits

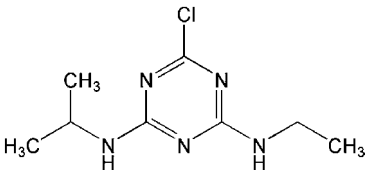
Cholesterol ($C_{27}H_{46}O$)

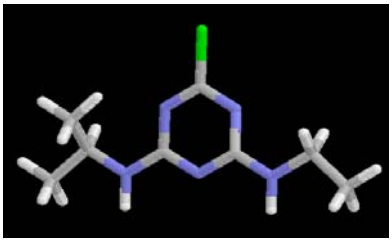




Cholesterol is a lipid that has a four linked hydrocarbon rings at its core (see sidebar).

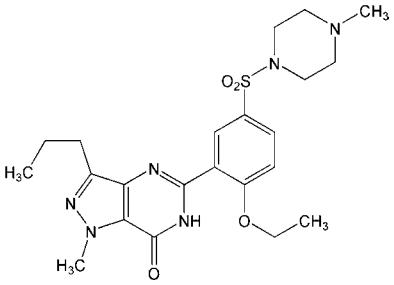
Atrazine ($C_8H_{14}ClN_5$)

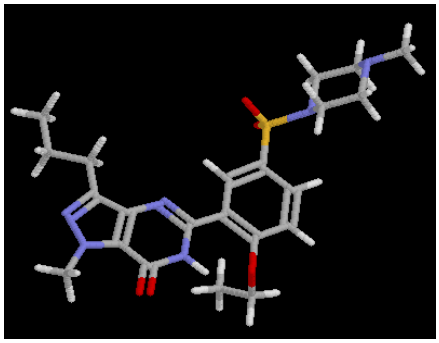




Atrazine is one of the most popular weed killers in the United States. Recent studies suggest that atrazine may be adversely affecting amphibian ecology.

Viagra ($C_{22}H_{30}N_6O_4S$)





Viagra (sildenafil citrate) is a vasodilator that is popularly prescribed for male erectile dysfunction (ED).

Discovery of Viagra

Viagra was an unexpected result of the search for a hypertension treatment.

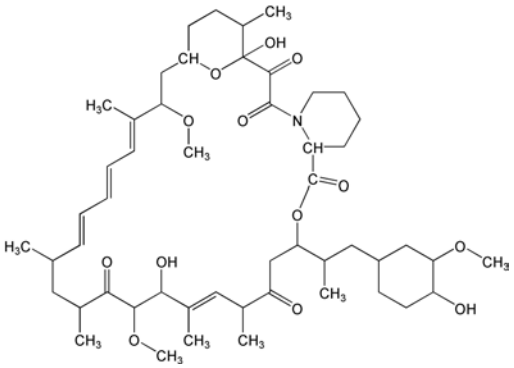
Increasing the level of cyclic-guanosine monophosphate (cGMP) relaxes the smooth muscle cells of the kidney and releases sodium, which in turn lowers blood pressure. To this end, scientists looked for ways to inhibit phosphodiesterases (PDEs), which normally convert cGMP to GMP.

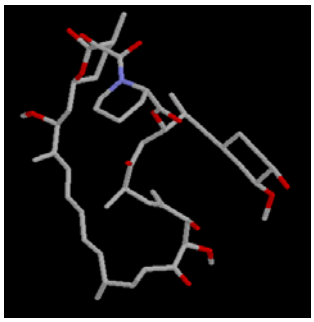
It turned out that there are many subtypes of PDEs in different tissues. PDE-5, for example, seemed to be involved in vasodilation. Some of the chemicals found were effective inhibitors of PDE-5, and thus showed promise as vasodilators. These drug candidates were tested to see if by increasing blood flow to the heart muscles, they could be used for treating chest pain and blood clot formation.

Viagra was a one of these PDE-5 inhibitors. It happened to work as a vasodilator primarily in the penis by increasing the arterial blood flow.

Molecules you can build with four kits

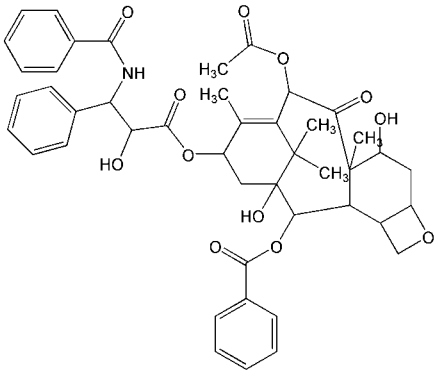
Rapamycin ($C_{51}H_{79}NO_{13}$)

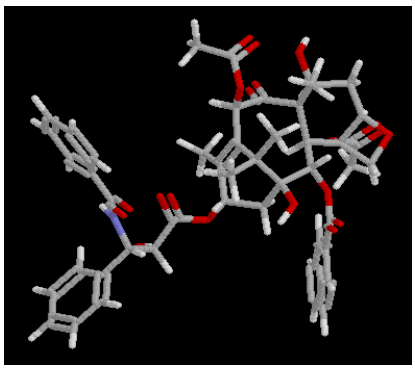




Rapamycin is an antibiotic. It has also shown promise as an immunosuppressive drug.

Taxol ($C_{46}H_{49}NO_{14}$)





Taxol (paclitaxel) is an anticancer drug.

Both rapamycin and Taxol were discovered as naturally occurring compounds.

Rapamycin was initially isolated as an antibiotic from a soil microorganism collected in Easter Island. (The name is derived from Rapa Nui, the local name for Easter Island.)

Taxol was originally isolated from the bark of the Pacific yew tree.

Making chemical drawings and 3-D models

There are many useful computer programs that make it easier to draw chemical structures.

The chemical drawings in this document were created in ChemDraw, popular commercial software sold by CambridgeSoft.

Alternatively, many more-economical shareware programs are available on the Web.

The 3-D structural images were made from molecular structural data in PDB (protein data bank) format, which is one of the popular standard 3-D chemical data file formats.

A variety of viewers can be used with the PDB file information. The images in this document were prepared by using RasMol or MDL Chime, two of the more popular 3-D molecular viewers.

About the Holiday Lectures on Science and Biointeractive

As part of its mission to strengthen science education, HHMI presents the Holiday Lectures on Science, an annual series that brings the latest developments in a rapidly moving field of research into the classroom. The lectures are given by HHMI investigators and other leading scientists. The 2002 Holiday Lectures, *Scanning Life's Matrix: Genes, Proteins, and Small Molecules,* are the tenth in the series, which began in 1993.

To complement the Holiday Lectures and enhance their usefulness in the classroom, HHMI produces a variety of free science education materials. Lecture summaries and key concepts, biographies of the lecturers, challenge questions and answers, and many other resources are available at www.holidaylectures.org. Videotapes, DVDs, and CD-ROMs can be ordered through HHMI's Online Catalog at http://catalog.hhmi.org.

The BioInteractive website (www.biointeractive.org) features virtual labs, animations, and other engaging instructional materials. They can be used to supplement the lecture topics or help teach about important concepts in the biomedical sciences.

The animations reveal hidden worlds and complex biological functions that cannot be easily conveyed via text alone or static illustrations. The virtual labs show science as a process while teaching key concepts and current methods and technology for laboratory investigation. The website also contains a virtual museum and many interactive resources.

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About the Howard Hughes Medical Institute

The Howard Hughes Medical Institute is a nonprofit medical research organization that employs hundreds of leading biomedical scientists working at the forefront of their fields. In addition, through its grants program and other activities, HHMI is helping enhance science education at all levels and maintain the vigor of biomedical science worldwide. Headquartered in Chevy Chase, Maryland, HHMI is one of the world's largest philanthropies, with laboratories across the United States and grants programs throughout the world.