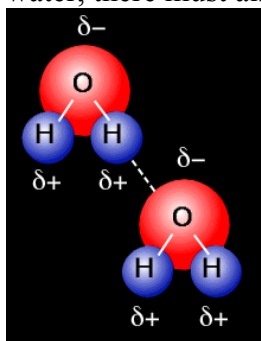


## 2.5 Solubility of Alkanes

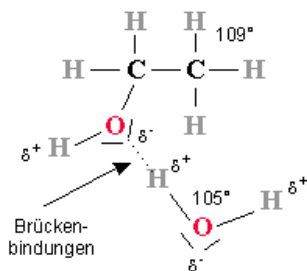
We learned in the chapter on solutions that “like dissolves like”: polar and ionic compounds are generally soluble in polar solvents like water, but not in non-polar (covalent) solvents like gasoline, oil, and (more biologically important) fat. Likewise predominantly non-polar (covalent) compounds are soluble in non-polar solvents, but not in polar solvents such as water.

The solubility of various organic molecules such as drugs, vitamins and hormones is of great physiological importance and we will be looking in substantial detail about the solubility of various biologically important organic molecules.

Recall that there are attractions between water molecules based on the attraction between  $\delta^+$  on the H atoms of one water molecule and  $\delta^-$  on the O of another water molecule. These attractive forces are called **hydrogen bonds**. For a substance to be soluble in water, there must also be attractions between that solute molecule and water molecules.



When we dissolve a polar or ionic compound into water, the same sort of attraction can occur; e.g. when we dissolve ethanol (ethyl alcohol) in water. This attraction allows ethanol to dissolve freely in water.



A similar situation occurs with methanol dissolved in water. Draw the arrangement that shows attractions between a methanol molecule and water.

A similar situation occurs with ammonia(NH<sub>3</sub>) dissolved in water. Draw the arrangement that shows attractions between an ammonia molecule and water.

If we look at the alkanes, there are no polar bonds in molecules containing only hydrogen and carbon and hence there is no attraction between alkane molecules and water molecules. Do you think any of the alkanes are going to be soluble in water?

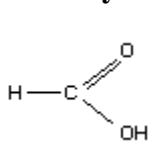
However solubility is not a black and white thing. Look at what happens to solubility (at 20°C) in the following series of molecules, each containing one polar OH group.

### Alcohol solubility in water

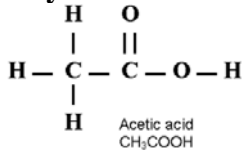
Solubility in H <sub>2</sub> O:	CH <sub>3</sub> OH complete(∞)	CH <sub>3</sub> CH <sub>2</sub> OH complete(∞)	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> OH complete(∞)
Solubility in H <sub>2</sub> O:	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> OH 12.5g/100ml	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> CH <sub>2</sub> OH 2.5 g/100ml	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> CH <sub>2</sub> OH 0.6 g/100 mL

(∞ is used as shorthand for completely soluble)

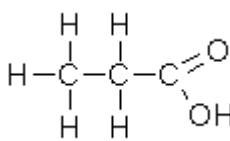
### Carboxylic acid solubility in water



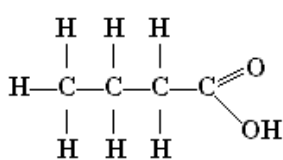
Complete



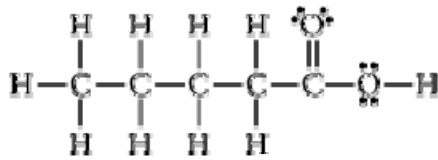
complete



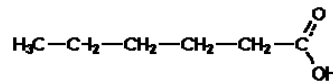
complete



5.62 g/L



3.7 g/L



0.4 g/L

### Carboxylate ions and ammonium ions

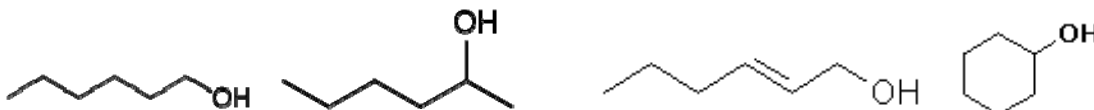
Carboxylate ions and ammonium ions tend to be completely soluble in water up to a length of approximately 16-18 C atoms. Evidently ionic groups are substantially more hydrophilic than polar O-H and N-H groups. Conversely **compounds with ionic groups are not at all soluble in very non-polar solvents such as hexane**, gasoline, and biological membranes.

The water solubility data of compounds above can be combined with data for some other polar functional groups as shown in the chart below

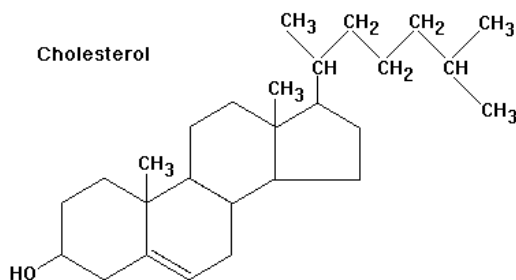
Number of C's	1	2	3	4	5	6
Functional group						
Alcohol	$\infty$	$\infty$	$\infty$	12.5	2.6	0.6
Carboxylic acid	$\infty$	$\infty$	$\infty$	5.62	3.7	0.4
Ketone	$\infty$	$\infty$	$\infty$	35	4.7	1.4
Amine	$\infty$	$\infty$	$\infty$	$\infty$	$\infty$	1.2
Amide	$\infty$	$\infty$	$\infty$	16		
Carboxylate ion	$\infty$	$\infty$	$\infty$	$\infty$	$\infty$	$\infty$
Ammonium ion	$\infty$	$\infty$	$\infty$	$\infty$	$\infty$	$\infty$

$\infty$  means completely soluble in water. Solubilities listed above are in g/L (Data from CRC Handbook of Chemistry and Physics)

As a general rule of thumb we can observe that the polar groups listed in the chart can solubilize a non-polar chain up to a length of around four to five  $\text{CH}_2$  units (including the C with the polar group).. The solubility is not affected significantly by the position of the polar group in the molecule or the presence of rings or  $\text{C}=\text{C}$  bonds.

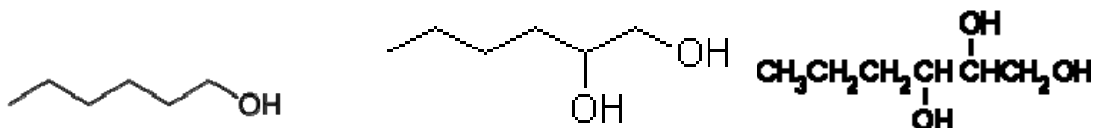


All four of the above molecules have one polar OH group and a nonpolar chain 6 C atoms long and they all have low solubility in water, on the order of a gram/L. All of them are more soluble than cholesterol, with structure shown below. Cholesterol has one polar OH group and a non-polar C chain of 25 C atoms!



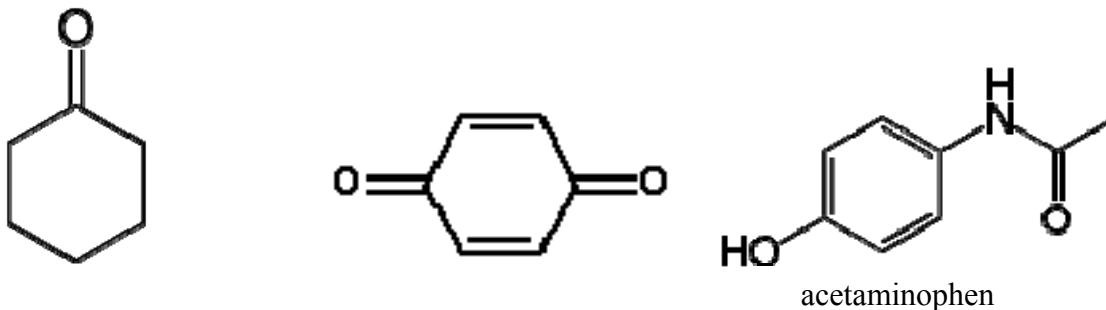
There are substantial variations in molecules with complex structures and real experimental data is always the final word, but we can make predictions on the solubility of a compound by counting the ratio of nonpolar  $\text{CH}_2$ 's to polar functional groups. If the ratio is less than 4 it will probably be quite soluble in water (and the smaller the ratio, the

more soluble it will be). Molecules with 5 or more CH<sub>2</sub> units per OH or other polar group will not be very water soluble, and the larger that ratio is, the less soluble it will be.



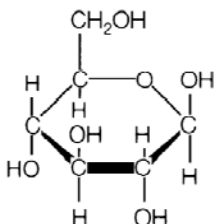
All of the above molecules have a 6 C chain but the first one has 1 OH group, the second molecule has 2 OH groups and the third one has 3 OH groups. Thus the nonpolar C/OH ratio in the first molecule is 6:1; the second molecule has a 6:2 or 3:1 C/OH ratio; the third molecule has 6:3 or 2:1 nonpolar/polar ratio. One can make the reasonable prediction that the first molecule will have low solubility in water, the second one will be quite soluble in water and the third one will be very soluble in water.

Predict the solubility of the following molecules in water:



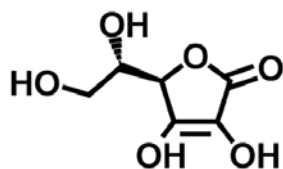
Answer: The first molecule has one polar ketone group on a 6-membered ring while the second molecule has 2 polar groups on the 6 membered ring. One will predict that the first molecule will have low solubility, similar to the previous cyclohexane with an OH group, while the second molecule will be quite soluble in water. Acetaminophen has 2 polar functional groups (OH and amide—treat the amide as one polar group). for 8 C atoms or a  $8/2 = 4:1$  ratio and would be predicted to be moderately soluble in water.

One can often predict the water solubility of complex biological and medically important molecules by looking at their structures and assessing the number of polar groups compared with the number of C's in nonpolar bonds. For example:



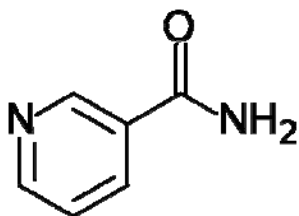
Glucose is the sugar found in blood and it is easy to see why it is very soluble in water. Every C has a polar OH group on it.

### Water soluble vitamins

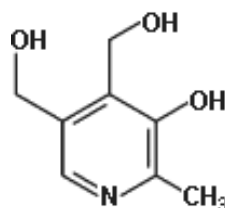


Ascorbic acid(Vitamin C)

Likewise ascorbic acid has a polar group on every C.



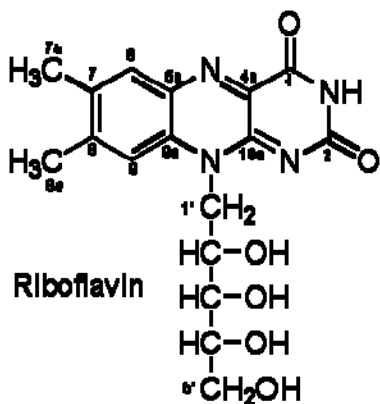
Nicotinamide(vitamin B3 )



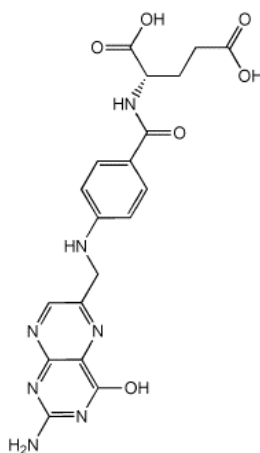
pyridoxine(Vitamin B6)

Nicotinamide has a polar amide group and a polar N-C bond in the 6-membered ring and 6 C units in the ring, giving a 6:2 nonpolar to polar ration and a prediction that it will be soluble in water. Pyridoxine is even more polar with 3 polar OH groups, a polar C-N bond and 8 nonpolar C units.

Without trying to do a precise count of polar groups vs nonpolar units, you should be able to “eyeball” the structures of the molecules below and conclude that there are enough polar groups to makes these molecules quite water soluble.



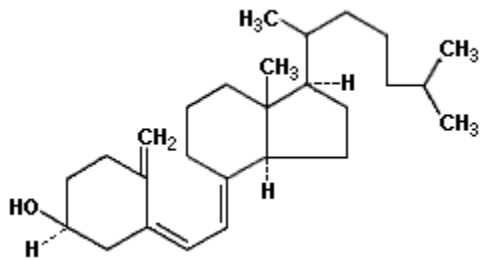
Riboflavin(B2)



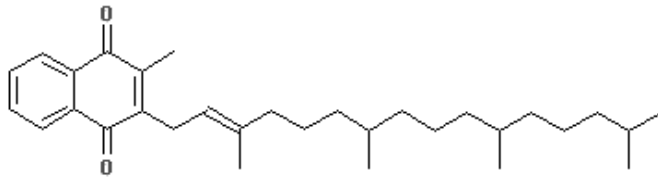
Folic acid

Ascorbic acid, nicotinamide, thiamine, riboflavin and folic acid are all classified as water soluble vitamins, with good reason.

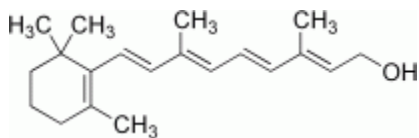
### Fat soluble vitamins



Vitamin D<sub>3</sub>



vitamin E



vitamin A (retinol)

Although the above three vitamins all have one or more polar groups, they have a much larger structure that is non-polar. Hence these molecules as a whole are not water soluble and are much more soluble in non-polar fat. They are in fact referred to as **fat soluble vitamins**.