kosmetikos*

SMELLS GREAT! WHAT'S THE CLOG P?

"The composition comprises from about 0.01% to about 1% by weight of the composition, of perfume wherein the perfume preferably comprises ingredients having a Clog P of 3 or smaller[1]."

Ah, Clog P! Nothing enhances the romance, the mystery, the aura of a fragrance more than the calculated logarithm of its water/octanol partition coefficient.

Most laboratories have amber bottles of perfume scattered about, composition unknown. Yet those odoriferous bottles contain—chemicals! Yes, those same atoms formed in the big bang, the heavy elements spewed forth during the death spasms of long departed stars, are milling about in that vessel.

Fragrance chemistry[2] is a vast and complex field. The chemical types present in fragrances are far more diverse than those comprising a typical personal care base. The label on a shampoo may contain a dozen or so ingredients—primary surfactant, secondary surfactant, foam and viscosity boosters, preservatives. Meanwhile, the fragrance can easily have fifty or a hundred materials—aldehydes, alcohols, ketones, heterocyclics, schiff bases, esters, etc.

Sitting undisturbed in its bottle, the chemistry of a fragrance is evolving[3]. The effect of fragrance on emulsion systems[4,5] or surfactant systems[6] is well known. Parsing the fragrance into its components and following its partitioning into the base will cast a bright light on the aesthetic and systemic effects. The nuances of solubility and surface activity of the component molecules cumulatively determine the effect of the vehicle on the fragrance impression[5]. From a pragmatic view, adjusting a perfume for a specific base is termed "translation," well described in reference 7.

Three decades ago, the physical properties of perfume were thoroughly explored in an extensive series of articles by Appell[8]. The bare list of subjects dealt with in these articles indicates how extensively pure science can be brought to bear on aroma chemistry: volatility, odor intensity, vapor pressure, odor tonality, minimum perceptible odor, odorimetric methods, equivalent weights of aromatic products.

The growth of technology since Appell wrote can bring new tools to bear on fragrance as science. Fragrance chemistry can serve as an entry into the computer analysis of functional behavior. The patent quoted at the beginning of this column holds a key—Clog P. Let's take a few steps back, technically speaking, to see where this strange creature came from.

The simplistic dichotomy of solubility, water or oil, was refined by Hildebrand[9] with the introduction of the solubility parameter (SP). The solubility parameter is a measure of all the cohesive properties of a molecule. Typical cosmetic ingredients fall in the range of 7 to 24, while fragrances have a somewhat smaller range, 8 to 13.

The SP range of aroma chemicals would indicate diverse behavior. β-pinene has an SP of 8.03, close to mineral oil at 7.75. Benzyl alcohol, at 12.31, is more water-compatable than propylene glycol at 11.78. Another approach of analyzing fragrance ingredients was proposed by Bonadeo[10]. A parameter was introduced, the "hydrophilic value" K_d, which could be related to the required HLB of aromatics used in cosmetics. This method assumes the fragrance to be part of the fatty ingredients of the emulsion—one aspect, surely, but not the whole story.

Lately, computer analysis has opened new possibilities for extracting physical properties from the molecular structure, including solubility characteristics. This is an aspect of an exciting new discipline, **QSAR** (**Q**uantitative **S**tructure-**A**ctivity **R**elationship theory). Using QSAR, perfume chemistry can be brought to the frontiers of modern chemical analysis.

The input of chemical structures into a

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Sidebar 1 SMILES[12]

SMILES is an acronym for Simplified Molecular Input Line System. It is a chemical notation system used to represent a molecular structure by a string of symbols. Aliphatic atoms are entered in upper case, aromatics are lower case. With rare exceptions, hydrogen is not notated. Single bonds are not shown:

Compound	Molecular Formula	SMILES
Methane	CH_4	C
Propane	CH_3-CH_2-CH_3	CCC
Ethanol	CH_3-CH_2-OH	CCH

A double bond is =, a triple bond is #:

Compound	SMILES
Propylene	C=CC
Propyne	C#CC

Branches are indicated by parentheses. More than one notation is possible for branched compounds. Different versions of isobutyric acid include: CC(C)C(=O)O and O-C(O)C(C)C. Cyclic structures use numbers to indicate where the ring starts and stops. Naphthalene can be c12ccccc1cccc2, showing the first carbon to be connected to the other 2 numbered carbons. For a more thorough discussion of SMILES, see reference 12.

computer program necessitates a new descriptive language. Several have been developed, but the most common may be **SMILES** (**S**implified **M**olecular **I**nput **L**ine **E**ntry **S**ystem), briefly sketched in sidebox 1. Take a perfume ingredient, find the chemical structure, convert it to SMILES, put it in the appropriate program, and you get Clog P!

Oops, we skipped a few steps! **Clog P** (**C**alculated **L**og of the octanol/water **P**artition coefficient) is a measure of water or oil compatibility. The octanol/water partition coefficient is the ratio of the equilibrium concentration in octanol and in water[1]. An ingredient with a smaller P is more hydrophilic, a larger P is more hydrophobic.

The patent requires fragrances with a P of 1000 or less. Since this is too big a number for the average technical person, the logarithm is used. Thus a log P of 3 or less is desired. The patent refers to fabrics, but we all know how wool is like hair—and hair is like skin (well, kinda...), so the application into personal care is self-evident.

Actually, Saunders[11] explored this concept in the early computer era, showing how odor perception is distorted by the polarity of the substrate. A gas chromatography procedure was employed to identify a correction factor for each ingredient to adjust for the varying polarities of substrates.

That leaves the C in Clog to explain. It isn't too hard to measure partition coefficients in the lab, but there are thousands of chemicals to look at, so using a computer that can pop out a value in a microsecond for any molecule you can imagine is quite convenient. Thus, the C stands for a calculated log P, as opposed to an experimental result. The process of finding Clog P for the perfume ingredient, vanillin, is shown in sidebox 2.

Some of the mystery is now gone from fragrance as an ingredient in personal care and household products, but this mystery only surrounded certain chemical properties. The knowledge of the Clog P of a perfume does yield some of its characteristics, but not the ultimate understanding of the power of scent. The magic of fragrance remains in its psychological and physiological effects, the complexities of which have only begun to be unravelled. ■

References

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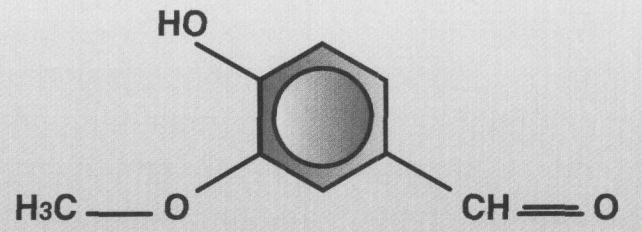
13. *http://clogp.pomona.edu/chem/clogp/drugs/html/vanillin.html*

Sidebar 2 CLOG P OF VANILLIN[13]

The SMILES notation for vanillin is COc1cc(C=O)ccc1O.



The log P contributions of the different fragments are:

Description	Value
Ether	-0.610
Aldehyde	-0.420
Hydroxy	-0.440
Aliphatic carbon	0.195
Aromatic carbons	0.780
Hydrogens	1.362
Chain bonds	-0.120
Potential interactions within ring	0.778
Normal ortho interaction	-0.250
Total	1.275

The reference for this data is a collection of the Clog P values of various drugs. Naturally, all this research was not initiated by fragrance or consumer goods companies. The research was funded by EPA and NIH owing to the medical and environmental importance of such analytical procedures. As an example of a medical application, the partition characteristics of a drug can predict its potential to accumulate in fatty tissue. Environmentally, it can predict the diffusion of water pollutants into fish. There is thus significant relevance for Clog P data in a wide range of disciplines.