ACCADEMIA DELLE SCIENZE
DELL'ISTITUTO DI BOLOGNA

ORDINE INTERPROVINCIALE
DEI CHIMICI DELL'EMILIA ROMAGNA

Sostanze naturali e alimenti funzionali

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Sostanze naturali e alimenti funzionali

1- Sostanza naturale = sostanza sicura e utile per la salute

2- Sostanza (chimica) sintetica = pericolosa per la salute

3- Quale è la differenza tra una molecola "naturale" e di "sintesi"

4- Alimenti funzionali: additivi?

Sostanze naturali: definizione

- ✓ **Le sostanze naturali sono composti chimici prodotti da un organismo vivente presenti in natura che svolgono una funzione biologica e possono avere un'attività terapeutica- farmacologica .**

- ✓ **Sebbene i prodotti naturali o farmaci hanno attività farmacologica, alcuni prodotti possono essere tossici ed avere effetti avversi per l'uomo**

- ✓ **Pertanto i prodotti naturali come per esempio molte tossine possono mostrare un doppio ruolo.**

Possibili effetti avversi o tossici

- ✓ **Tossicità intrinseca di componenti del prodotto o di loro metaboliti in funzione della dose assunta**
  - ***Molti estratti o principi attivi naturali vengono assunti a dosi giornaliere molto alte (grammi) mai utilizzate nel passato***
- ✓ **Inproprie procedure di estrazione, purificazione e utilizzo di metodologie chimico-analitiche non appropriate per la loro caratterizzazione e certificazione.**
  - ***Sostanze naturali importate da paesi con scarse e non validate normative di qualità: certificati di analisi chimica relativo alla purezza non appropriato e utilizzo metodologie analitiche opsolete non in grado di definire la purezza del composto e le relative impurezze***
- ✓ **Contaminazione accidentale** ***(es. tossine microbiche, metalli, pesticidi, microrganismi) o*** **intenzionale** ***(es. sostituzioni con sostanze simili non appropriate)***
- ✓ **Interazioni tra diverse sostanze naturali e farmaci assunti dal soggetto**

Possibili effetti tossici

Direttiva 2004/24/EC istitusce una procedura di registrazione semplificata per i medicinali vegetali che soddisfano determinati requisiti, tra i quali:

"in seguito al suo impiego tradizionale, il prodotto ha dimostrato di non essere nocivo nelle condizioni d'uso indicate".

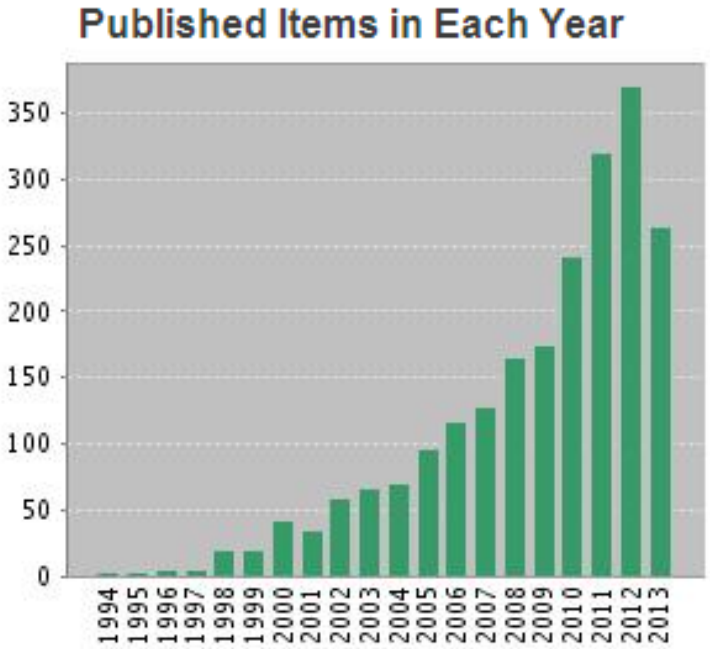
Distribuzione?
Biodisponibilità?
Attività organo-specifica?
Metabolismo (dose-dipendente)?
Tossicità (diretta, metaboliti)?

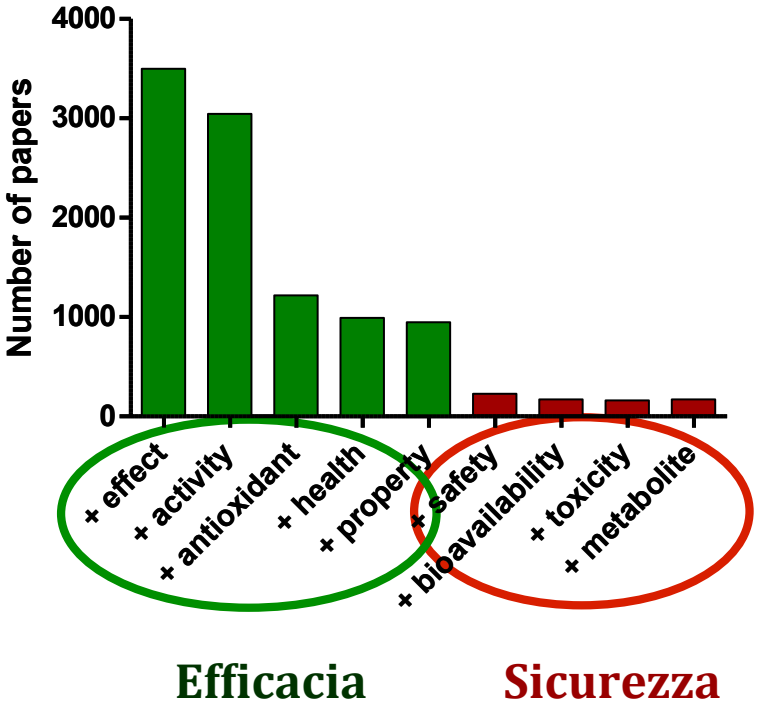
ADME (assorbimento, distribuzione, metabolismo ed eliminazione della/delle molecole somministrate) ?

Risposta soggettiva?

ISI Web of Knowledge (http://apps.webofknowledge.com/)

Topic=(nutraceutical)_8068 articles (accessed September 2013)





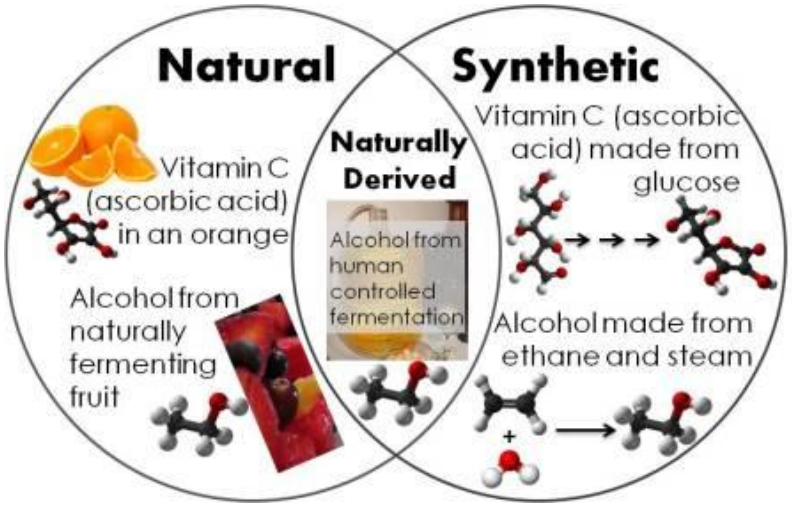
Possibili effetti avversi o tossici: cosa fanno in giro per il mondo?

Food Standards Australia New Zealand refers to novel food **as "*a non-traditional food*"** for which there is insufficient knowledge in the broad community to enable safe use in the form or context in which it is presented, taking into account:

a) The composition or structure of the product;
b) Levels of undesirable substances in the product;
***c)** Known potential for adverse effects in humans;*
d) Traditional preparation and cooking methods; or
e) Patterns and levels of consumption of the product";

In general a ***non-traditional food*** is defined as: "**A food which does not have a history of significant human consumption by the broad community in Australia or New Zealand".**

Sostanze chimiche di sintesi : definizione

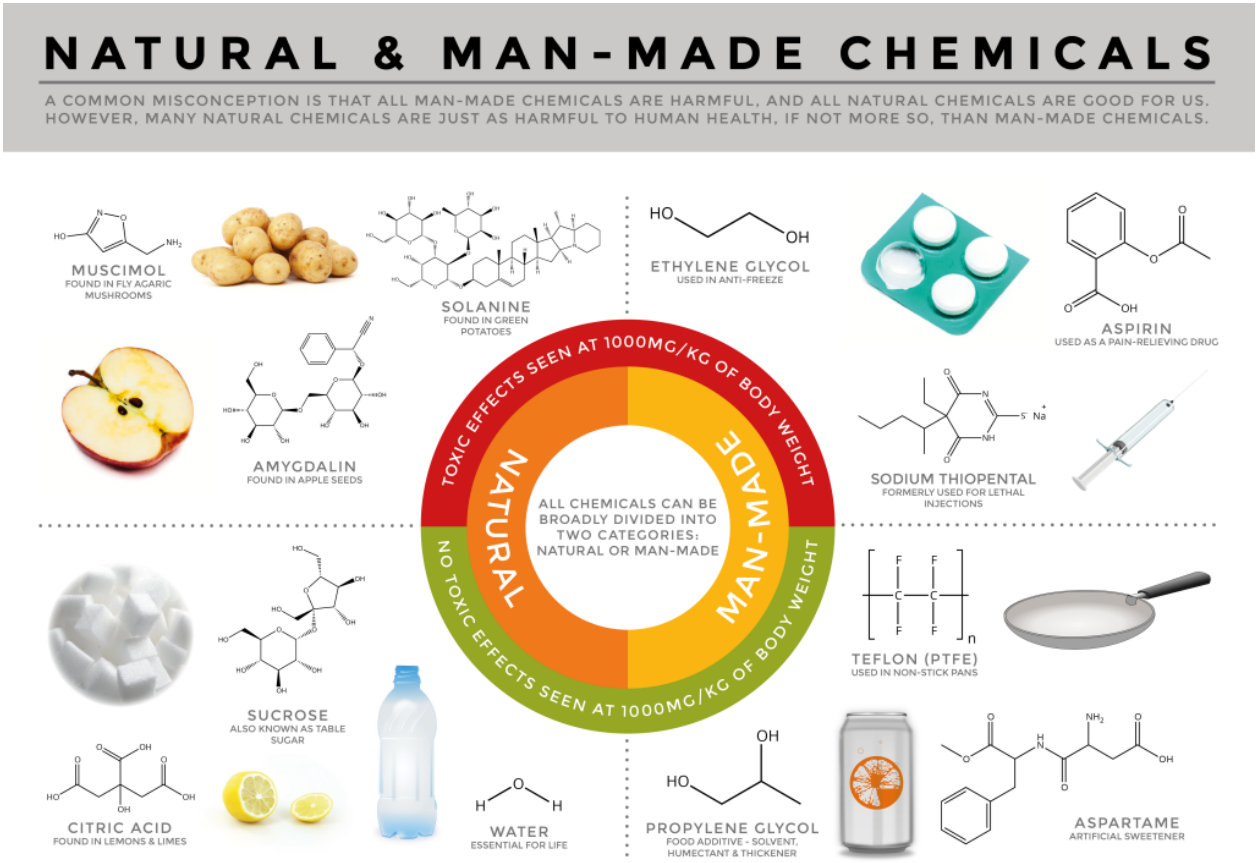


Natural vs. Synthetic Venn Diagram

Natural chemicals are produced by nature without any human intervention. **Synthetic chemicals are made by humans using methods different than those nature uses, and these chemical structures may or may not be found in nature**. This definition means a synthetic chemical can be made from a natural product (i.e. naturally derived).

Note that in the food industry, "artificial" is used instead of "synthetic"

The term '**chemophobia**' has been used on social media amongst chemists with increasing regularity over the past year and refers to the growing tendency for the public to be **suspicious and critical of the presence of any man-made (synthetic) chemicals in foods or products that they make use of**.



Natural versus synthetic chemicals Is a Gray Matter

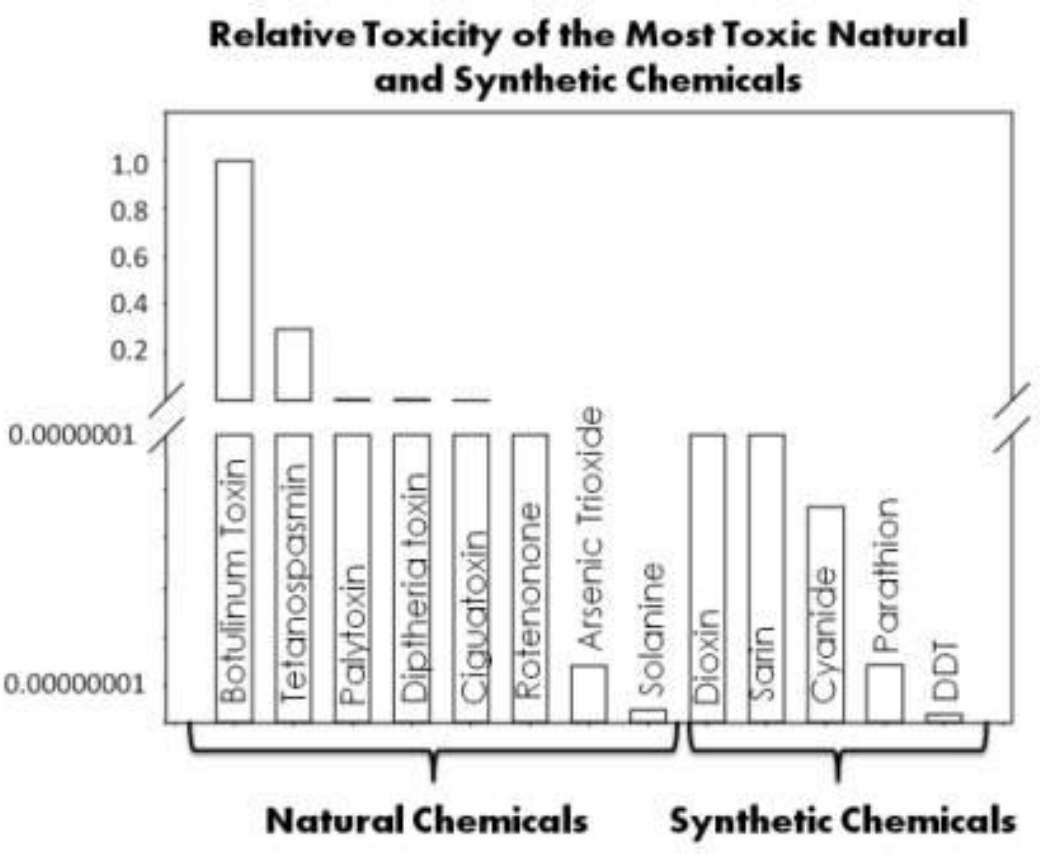
We consumers are bombarded with advertisements for natural and organic products. There are websites and news stories beyond counting dedicated to sharing the following message: **"man-made is bad and natural is good".** The growing popularity of this belief shows that this subject is in dire need of clarification.

The most common misunderstandings about natural and synthetic chemicals are:

1. **Synthetic chemicals are more toxic than natural chemicals.**
2. **Organically grown food is better for you because it's all natural.**
3. **Synthetic copies of natural chemicals are not as good for you.**

Misconception 1: Synthetic chemicals are more toxic than natural chemicals.

The two most toxic chemicals for humans, that we know of, are botulinum toxin and tetanospasmin. Botulism is caused by botulinum toxin, which is a protein and neurotoxin produced by bacteria spores. Tetanospasmin is a neurotoxin produced by bacteria that causes Tetanus.



"Among the agents identified as human carcinogens by the International Agency for Research in Cancer 62% occur naturally: 16 are natural chemicals, 11 are mixtures of natural chemicals, and 10 are infectious agents. Thus, the idea that a chemical is "safe" because it is natural, is not correct"

The Most Toxic Chemicals to Humans Are Natural!

Natural Chemicals

Chemical Name	LD_{50} (mg/kg)	1 / LD_{50}	Relative Toxicity
Botulinum toxin (aka Botox)*	3.00E-07	3.33E+06	1.00E+00
Tetanospasmin***	1.00E-06	1.00E+06	3.00E-01
Palytoxin*	5.00E-05	2.00E+04	6.00E-03
diphtheria toxin***	1.00E-04	1.00E+04	3.00E-03
Ciguatoxin*	2.50E-04	4.00E+03	1.20E-03
Batrachotoxin*	2.00E-03	5.00E+02	1.50E-04
Saxitoxin*	3.40E-03	2.94E+02	8.82E-05
Tetrodotoxin*	0.01	1.00E+02	3.00E-05
Ricin**	0.03	3.33E+01	1.00E-05
Alpha-Amanatin*	0.1	1.00E+01	3.00E-06
Muscarine*	0.23	4.35E+00	1.30E-06
Aflatoxin*	0.3	3.33E+00	1.00E-06
Strychnine*	1	1.00E+00	3.00E-07
Rotenonone*	3	3.33E-01	1.00E-07
Arsenic Trioxide*	15.1	6.62E-02	1.99E-08
Solanine*	67	1.49E-02	4.48E-09

Synthetic Chemicals

Chemical Name	LD_{50} (mg/kg)	1 / LD_{50}	Relative Toxicity
TCDD (the most toxic dioxin or PCB)*	0.022	4.55E+01	1.36E-05
Sarin*	0.42	2.38E+00	7.14E-07
Parathion*	4	2.50E-01	7.50E-08
Sodium cyanide*	15	6.67E-02	2.00E-08
DDT*	113	8.85E-03	2.65E-09

- LD_{50} is the lethal dose required to kill half the population studied, which means the smaller the number the more toxic it is
- $1/LD_{50}$ is the inverse of the LD_{50}
- The relative toxicity is making all the toxicities ($1/LD_{50}$) relative to the most toxic chemical, botulinum toxin

Sources
* Merck Index
** Winder, C., Toxin Reviews, 2004, Vol. 23, No. 1 , Pages 97-103
*** University of Florida, Environmental Health & Safety

Plants inherently also contain various harmful or toxic substances the purpose of which is, for example, to fend off the adverse effects of insects or different diseases, or to protect the plant against perishing.

Natural toxic substances in foodstuffs include:

- glycoalkaloids, such as solanine in potatoes and tomatine in raw tomatoes
- nitrates in vegetables
- gyromitrin in false morels
- lectins in beans
- coumarin in cinnamon
- biogenic amines in fruits and vegetables
- cyanoglycosides in fruit seeds and stones and in cassava.

Although many foods contain toxins as a naturally-occurring constituent or, are formed as the result of handling or processing, the incidence of adverse reactions to food is relatively low

Misconception 2: Synthetic copies of natural chemicals are not as good for you.

The chemical structure of a synthesized compound is exactly the same as the natural compound it is supposed to supplement, such as ascorbic acid, which is the primary form of Vitamin C.

It will taste the same, smell the same, and it will function the same in your body.

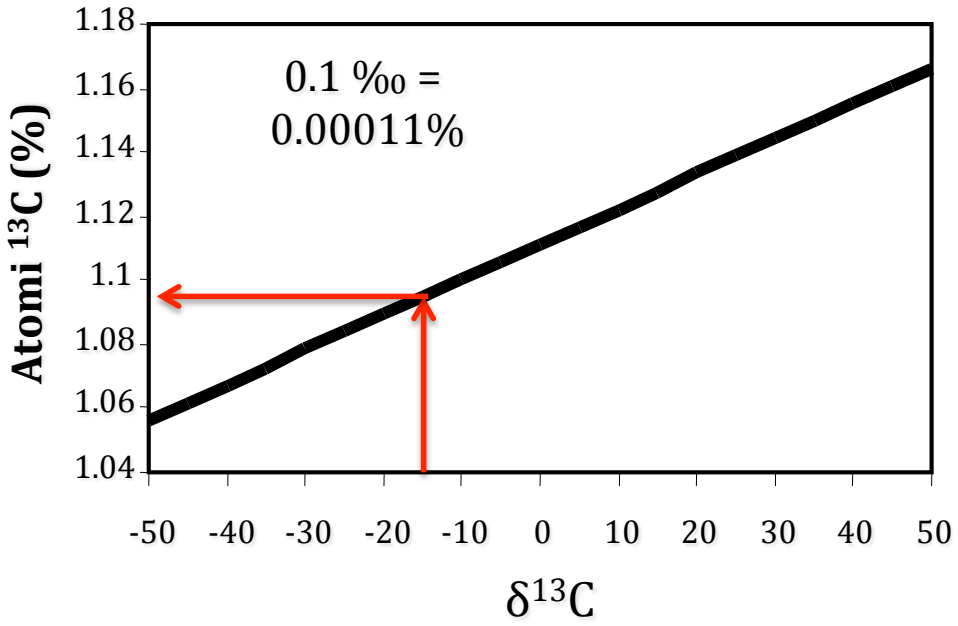
The only differences among synthetic and natural substances is in the isotopic abundance of the different atoms:

- ^{1}H: 99.984% ^{2}H o D: 0.01557%
- ^{12}C: 98.89 % ^{13}C: 1.11140%
- ^{14}N: 99.64% ^{15}N: 0.36630%
- ^{16}O: 99.76% ^{17}O: 0.04% ^{18}O: 0.20004%
- ^{32}S: 95.02% ^{33}S: 0.75% ^{34}S: 4.21500% ^{36}S:0.02%

Isotope Ratio Mass Spectrometry:IRMS

- Per esprimere i risultati di misure di rapporto isotopico del carbonio, si utilizza generalmente la grandezza $\delta^{13}C$ definita come differenza relativa (in ‰) tra il rapporto $^{13}C/^{12}C$ del campione e quello di uno standard di riferimento (*Belemnitella americana* con $^{13}C/^{12}C$ pari a 0.011237.

$$\delta^{13}C = \left(\frac{^{13}C/^{12}C_{(\text{campione})}}{^{13}C/^{12}C_{(\text{standard})}} - 1 \right) \times 1000$$



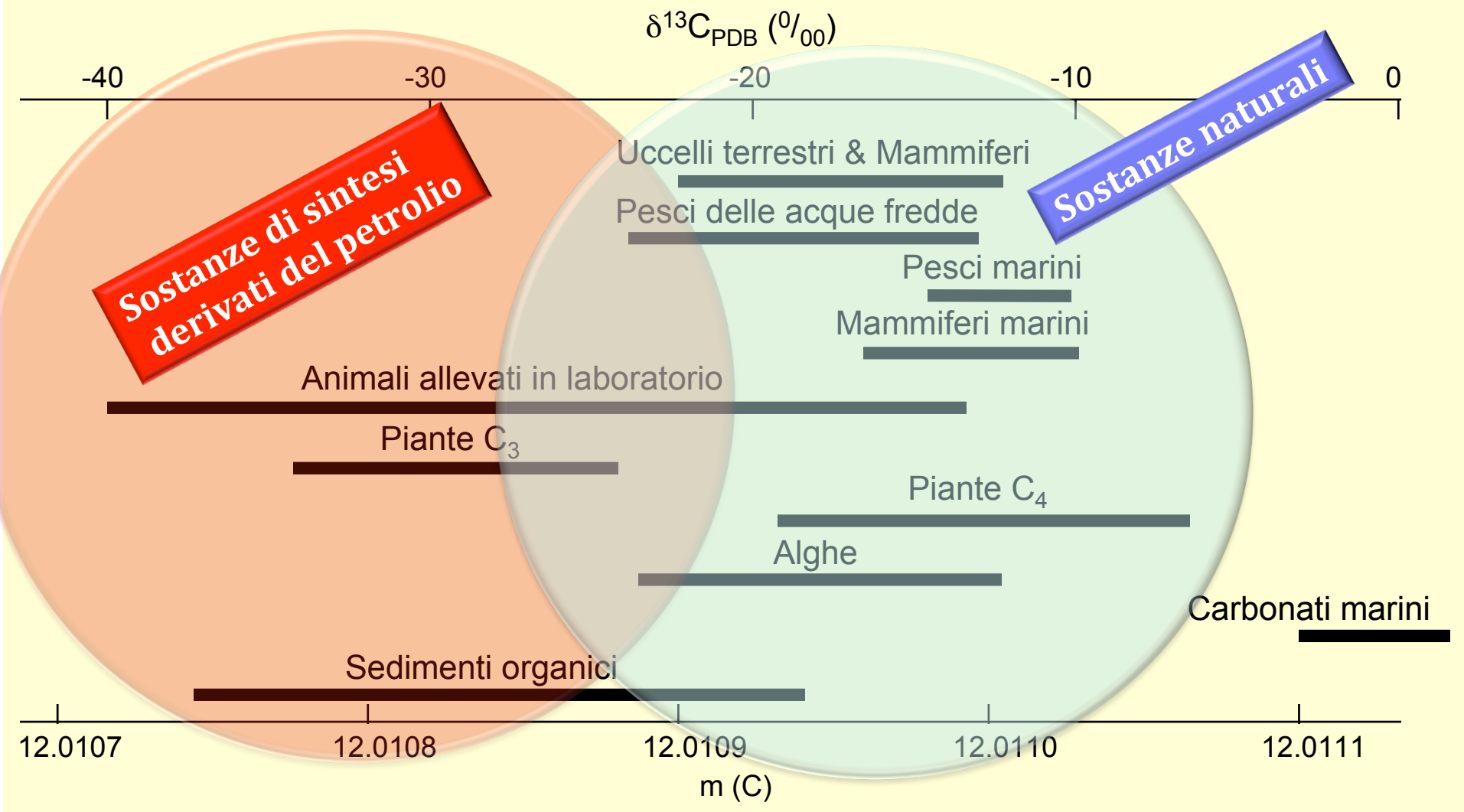
Il rapporto isotopico $^{13}C/^{12}C$ può fornire utili informazioni analitiche:

- Esiste una notevole differenza di tale rapporto tra piante con ciclo fotosintetico C_3 e quelle con ciclo fotosintetico C_4 e tutte le sostanze estratte e prodotte da questi vegetali presentano un rapporto $^{13}C/^{12}C$ riferibile al vegetale stesso;
  per esempio, il glucosio ottenuto dalla canna da zucchero (pianta C_4 δ=-11‰) e quello dalla barbabietola (pianta C_3 δ=-25‰) presentano un rapporto $^{13}C/^{12}C$ significativamente diverso.

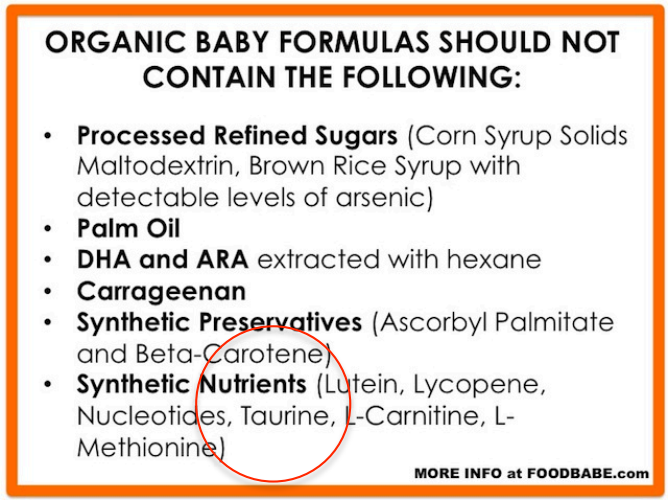
- Esistono poi differenze nelle sostanze di provenienza terrestre rispetto a quelle marine e differenze tra sostanze naturali e sintetiche.

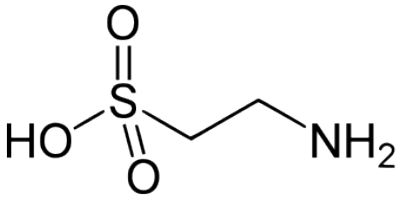
- Tutti i derivati del petrolio presentano un $\delta^{13}C$ intorno a -31‰, potenzialmente utile per una loro identificazione in altre matrici.

$\delta^{13}C$ Rapporto isotopico $^{13}C/^{12}C$ di molecole derivanti da diverse origini



Sinthetic VS Natural Taurine





Taurine is an export-oriented product in China, almost 90% of the global taurine is produced by China, which is mainly exported to the US, Europe and Japan.

Natural taurine is obtained from ox bile by alcaline hydrolysis of taurine amidated bile acids:

δ=-15.40‰

Synthetic taurine is obtained from 2-hydroxyethanesulfonic acid, which in turn is obtained from the reaction of ethylene oxide with aqueous sodium bisulfite.

δ=-26.60‰

10.000 taurine molecules contain:

- Synthetic: 110 atoms C 13, 9890 atoms C 12
- Natural: 108 atoms C 13, 9892 atoms C 12

La differenza è di 2 neutroni !!! e questa differenza è comune tra tutti i prodotti naturali di diversa origine

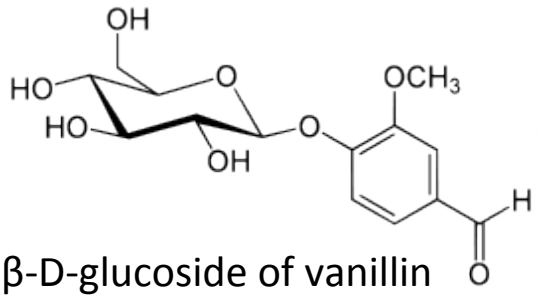
AM.Gioacchini, A. Roda, et all Differentiation between natural and synthetic taurine using the $^{13}C/^{12}C$ isotope ratio.

NATURAL VS. SYNTHETIC CHEMICALS

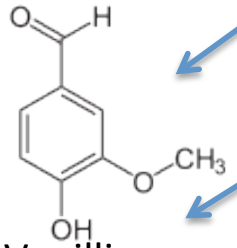
There's **natural vanilla** flavoring and there's **synthetic vanilla** flavoring. Is there a difference?

-Natural vanilla is exceedingly expensive: up to about **$7** dollars (US) per gram
-Synthetic vanilla extract: **$ 0.02** (US) per gram

Natural vanillin starts as this chemical in the green seed pods



β-D-glucoside of vanillin

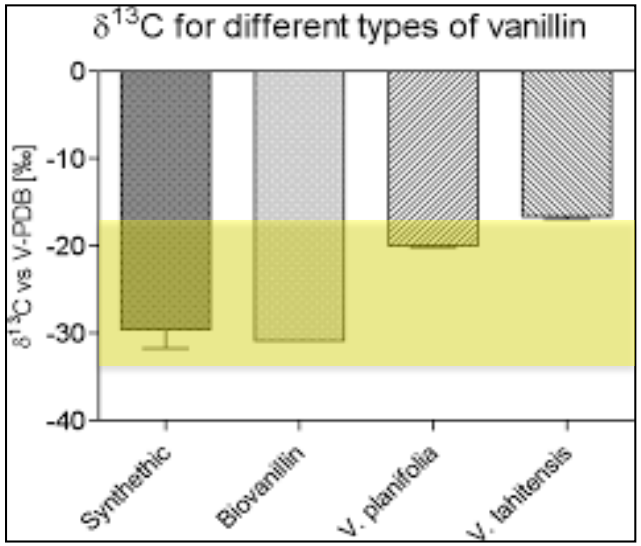


Vanillin

An easy method is to take 4-hydroxybenzaldehyde use a technique of electrophilic bromination and then copper-catalyzed methoxylation.

Using synthetic biology Evolva edit the DNA of yeast, and through a fermentation process, force it to synthesize vanillin

β-D-glucoside doesn't smell or taste anything like vanilla. After some super secret processes that involve leaving the green beans in the sun for a couple of weeks, the beans begin to smell like vanilla. The β-D-glucoside has broken down into vanillin.



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April 10, 2013

Have I convinced you that natural vs. Synthetic chemicals is a gray matter?

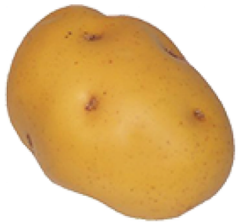
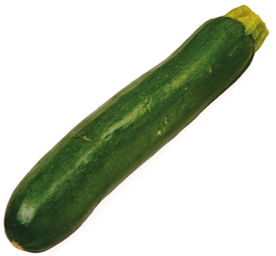
We all have to accept that the natural vs synthetic chemical debate is not **a black vs white issue**, and it is actually a complicated and massive gray matter.

Both natural and synthetic chemicals need to be considered on a case by case basis for our personal health, whether it's a drug, a food additive, or the pesticides being used on our crops.

Manmade or natural, tasty or toxic, they're all chemicals …

The terms 'chemical' and 'poison' have become interchangeable in the popular consciousness and as a result the whole subject of chemistry has become tainted with unpleasant connotations

"THE DOSE MAKES THE POISON"

APPLE SEEDS	PEARS	POTATOES	COURGETTES
			
CONTAIN AMYGDALIN ~0.6g/kg of seeds	CONTAIN FORMALDEHYDE ~0.06g/kg	CONTAIN SOLANIN ~0.2g/kg (higher in green potatoes)	CONTAIN CUCURBITACIN E Variable (higher in bitter courgettes)

ALL OF THE FOOD ITEMS ABOVE CONTAIN NATURAL CHEMICALS THAT ARE TOXIC TO HUMANS. HOWEVER, THEY ARE USUALLY PRESENT IN VERY SMALL AMOUNTS, FAR BELOW THE HARMFUL DOSE.

JUST BECAUSE A CHEMICAL IS PRESENT, DOES NOT MEAN THAT IT IS HARMFUL IN THE *AMOUNT* PRESENT.

Proc. Natl. Acad. Sci. USA
Vol. 87, pp. 7782–7786, October 1990
Medical Sciences

Nature's chemicals and synthetic chemicals: Comparative toxicology*

(carcinogens/mutagens/teratogens/clastogens/dioxin)

BRUCE N. AMES†‡, MARGIE PROFET†, AND LOIS SWIRSKY GOLD†§

ABSTRACT **The toxicology of synthetic chemicals is compared to that of natural chemicals, which represent the vast bulk of the chemicals to which humans are exposed. It is argued that animals have a broad array of inducible general defenses to combat the changing array of toxic chemicals in plant food (nature's pesticides) and that these defenses are effective against both natural and synthetic toxins. Synthetic toxins such as dioxin are compared to natural chemicals, such as indole carbinol (in broccoli) and ethanol. Trade-offs between synthetic and natural pesticides are discussed. The finding that in high-dose tests, a high proportion of both natural and synthetic chemicals are carcinogens, mutagens, teratogens, and clastogens (30–50% for each group) undermines current regulatory efforts to protect public health from synthetic chemicals based on these tests.**