



# Plant Cell Culture HTN™ Technology for High Quality & Sustainable Ingredients

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Genova

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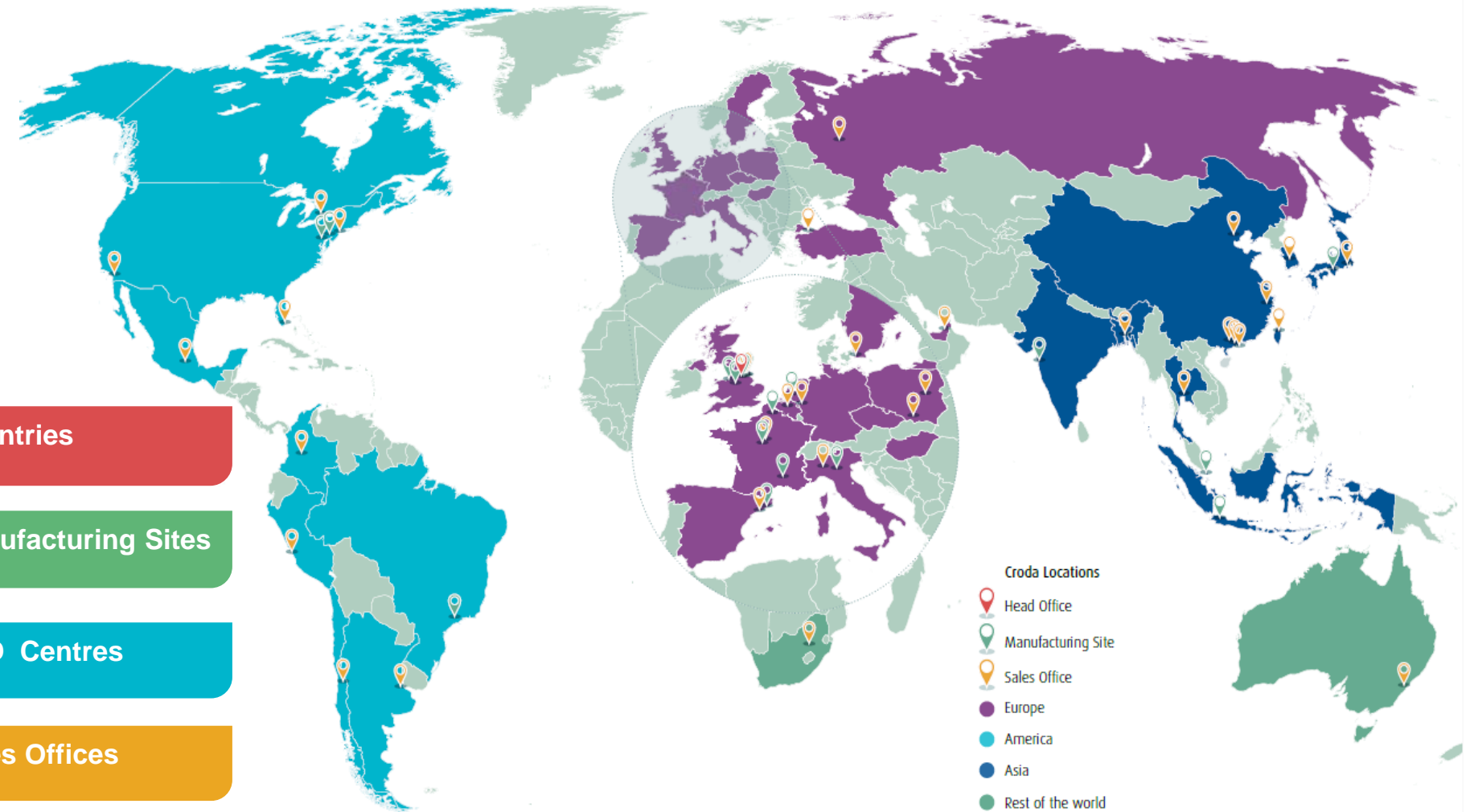
# Croda International is a global leader in speciality chemicals, from Personal Care to Health Care; from Crop Care to Coatings and Polymers

33 Countries

17 Manufacturing Sites

18 R&D Centres

32 Sales Offices



# Agenda

1. **Quality and safety and availability issues of botanicals for food use**
2. **HTN™ Technology: features and advantages**
3. **Echigena PluS™: the first biotech Echinacea angustifolia extract approved in Europe as food supplement ingredient**

# Quality and Safety of plant Active Substances have always been a problem

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The presence of **pollutants** as pesticides, heavy metals and aflatoxins is detected in many plant actives and extracts

SAFETY

Many problems due to difficult accessibility of plants compromise the **availability** of Natural Active Substances

AVAILABILITY

The **variability** in the concentration of active substances is a limit to the reproducibility of the biological effect

STANDARDIZATION

**ECO-SUSTAINABILITY**



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# Worldwide Authorities are concerned by Botanicals Safety & Quality issues



European Food Safety Authority

SAFETY

STANDARDIZATION

EFSA Journal 2009; 7(9):1249

## SCIENTIFIC OPINION

**Guidance on Safety assessment of botanicals\* and botanical preparations\*\*  
intended for use as ingredients in food supplements<sup>1</sup>**

**EFSA Scientific Committee<sup>2</sup>**

European Food Safety Authority (EFSA), Parma, Italy



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# Factors Affecting Echinacea Quality

Letchamo W. et al., Trends in new crops and new uses, 2002

## Mystery of “Green Colored” Extracts

The problem of “green colored” *E. angustifolia* hydroalcoholic extracts has been a matter of speculation since 1995 in North American herbal industry. In fact, most vendors (bulk suppliers of certified organically grown roots) regarded this feature as a positive attribute and even promoted it as a “uniquely useful property” in their marketing campaigns. In our 1996–1998 field investigations and laboratory analyses, we found that in some organic commercial fields, root rot affected about 55%–60% of the second and third year *E. angustifolia*, and 30%–38% of *E. purpurea* plants. As the disease progresses, roots change color to dark brown, while the leaves wilt and die back very slowly (Fig. 4). Though the root may be infected, the plants can still grow beyond the first and second years. In most cases, however, infected roots are harvested and processed for marketing. The problem of “green colored extract” was mostly prevalent in roots originating from the “certified organically produced” echinacea. After the first week following extraction, the green extracts developed



Healthy roots



Contaminated roots

**ROOT ROT:**  
fungal contamination  
from  
*Phymatotrichum  
omnivorum*

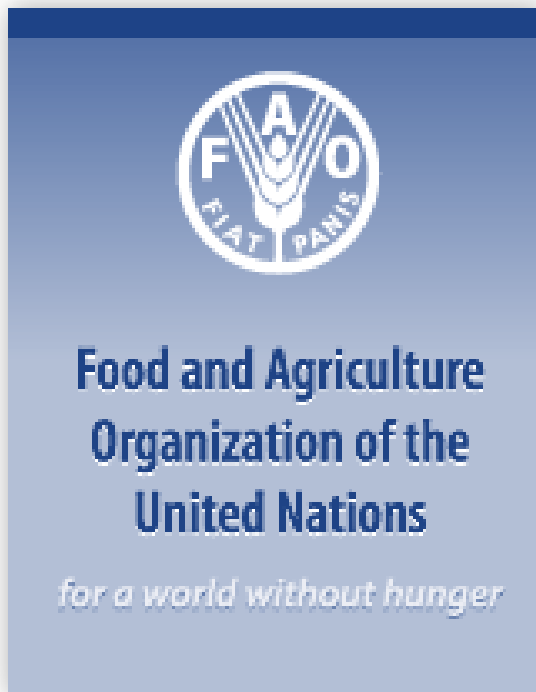
**CONTAMINATED ORGANIC ROOTS were associated with low levels of active substances**



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# Since 1994 Fao Endorsed Plant Tissue Culture Technology As A Reliable Alternative For The Production Of Food Substances

AVAILABILITY

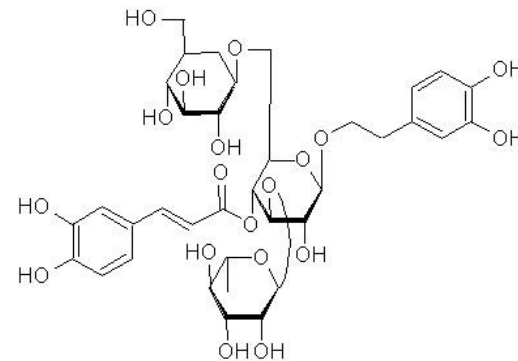


- ***“Plant cell culture is viewed as a potential means of producing useful plant products such that conventional agriculture, with all its attendant problems and variables, can be circumvented.*”**
- ***These problems include: environmental factors (drought, floods, etc.), disease, political and labour instabilities in the producing countries (often Third World countries), uncontrollable variations in the crop quality, inability of authorities to prevent crop adulteration, losses in storage and handling.”***



## Echigena Plus™: titered in Echinacoside

**Echigena Plus**, is the unique biotech *Echinacea angustifolia* cell culture extract titrated at **4% echinacoside**, approved for food use.



*Echinacea angustifolia* is a herbaceous plant native to **North America**, which is efficacious to heal **cold and flu** and as a **stimulant for the immune system**. These activities are provided by a variety of substances including polysaccharides and **echinacoside**, a phenolic compound belonging to the family of phenylpropanoids.

**The availability and standardization of these active substances from plant material is limited** thus contributing to the non definitive results so far obtained in clinical trials testing Echinacea immunoboosting efficacy (Barnes et al., 2005) on prevention and treatment of upper respiratory tract infections.



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# IRB HAS FOLLOWED FAO'S RECOMMENDATION

IT MAY BE A LEAF, A FLOWER OR A SEED. ONLY A SMALL AMOUNT OF PLANT TISSUE IS REQUIRED TO FIND SPECIFIC ACTIVE SUBSTANCES



Plant tissue



Sampling of sterilized tissues



Callus induction in solid culture



Callogenesis



New cell line



Selection



Scaling Up

Homogenization

Filtration  
Extraction



HIGHLY  
STANDARDIZED  
EXTRACTS



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# Highly distinctive advantages are offered by IRB green biotech approach



## Assuring 100%

- **SAFETY:** No environmental contaminants or crop adulteration since cells grow in a sterile medium which secures the absence of pesticides, heavy metals and aflatoxins
- **AVAILABILITY:** Full access to natural substances included rare and difficult to synthesize substances; Independence from crop yield with no price fluctuation
- **STANDARDIZATION:** batch-to-batch highest reproducibility (composition & efficacy); minor impact on taste and color of formulation
- **ECO-SUSTAINABILITY:** Totally eco-friendly approach and truly eco-sustainable with dramatic saving of natural resources



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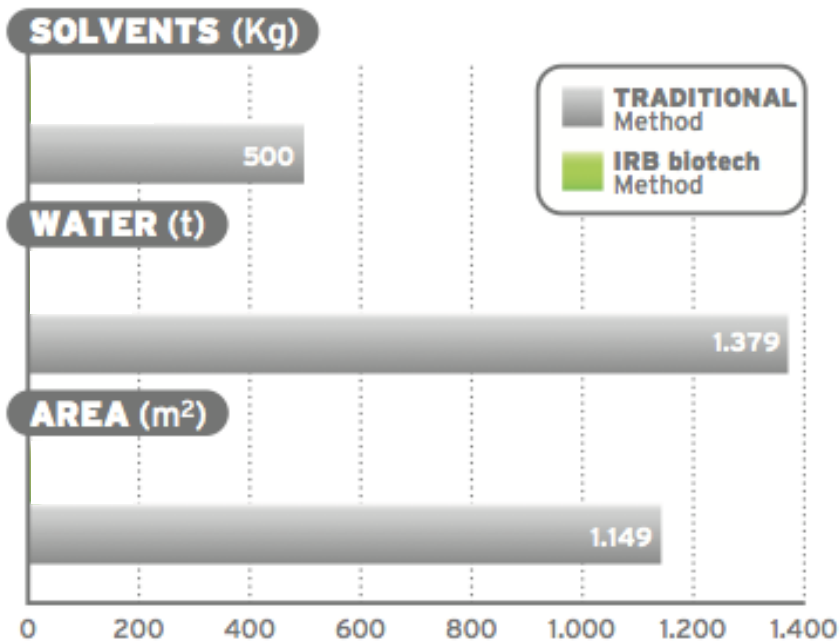
# Echigena PluS™

## Unrivaled Eco-Sustainability



*Echinacea angustifolia* is less common than the similar species *E. pallida* and *E. purpurea* because it's more difficult to grow on field.

The extraction of echinacoside requires almost a **3-year soil cultivation** before collecting roots which contain limited amounts of the active substance (max 2%).



Average use of solvents and natural resources for the production of **1 Kg of echinacoside** from *Echinacea angustifolia* with the **traditional method** and with the **IRB green biotech process**



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# Echigena PluS™

## Unrivaled Eco-Sustainability



HTN is an eco-sustainable **GREEN** biotech process:

- NEGLIGEABLE SOIL OCCUPANCY: SOIL CAN BE CULTIVATED FOR FOOD
- TREMENDOUS REDUCTION OF WATER AND SOLVENTS USE
- ABOLISHMENT OF FERTILIZER AND PESTICIDES
- NO IMPACT ON BIODIVERSITY
- NO IMPOVERISHMENT OF THE FLORA



2011 European Business Award for the Environment: **Best Process and Technology:**  
**WINNER** with HTN technology



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# IN 2009 TWO INNOVATIVE BIOTECH BOTANICALS ACHIEVED EUROPEAN AUTHORIZATION AS FOOD SUPPLEMENT INGREDIENTS

WINNER  
**noti**  
Nutraceutical  
Business &  
Technology  
Awards 2011



**ECHIGENA Plus™**



**TEOSIDE™ 10**

## THROUGH SUBSTANTIAL EQUIVALENCE

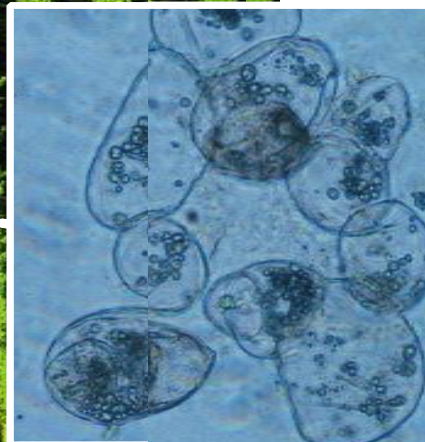
Novel food notification (article 5, EC n° 258/97)

When a new product is **essentially equivalent** in composition to an existing product, then it can be considered **as safe as its conventional equivalent**. (Joint Consultation FAO/WHO, 1996)



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**OTTIMIZZIAMO IN MICRO,  
MIGLIORIAMO IL MACRO.**



Thank you  
[www.irbtech.com](http://www.irbtech.com)

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# Back up

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# ECHIGENA PLUS™: PRODUCT SPECIFICATIONS



<b>Product composition</b>	Echinacea angustifolia (Asteraceae) cell culture extract titrated at 4% of echinacoside Excipients: organic maltodextrins
<b>Appearance</b>	amber-coloured powder with characteristic odour
<b>Solubility</b>	soluble in water (Eur. Ph. 5 <sup>th</sup> Edition)
<b>Preservatives</b>	absent
<b>Total aflatoxins</b>	absent
<b>GMO</b>	absent
<b>Pesticides</b>	absent
<b>Microbiological Specifications:</b>	Total microbial count: bacteria < 1000 UFC/g fungi < 100 UFC/g
<b>Packaging</b>	1 Kg
<b>Storage</b>	Store the product in the original, well closed container, in a cool, dry area and protected from light
<b>Shelf life</b>	24 months

## Daily dosage:

Anti-stress: 60-120 mg

Immunobooster: 150-300 mg

## Formulation tips:

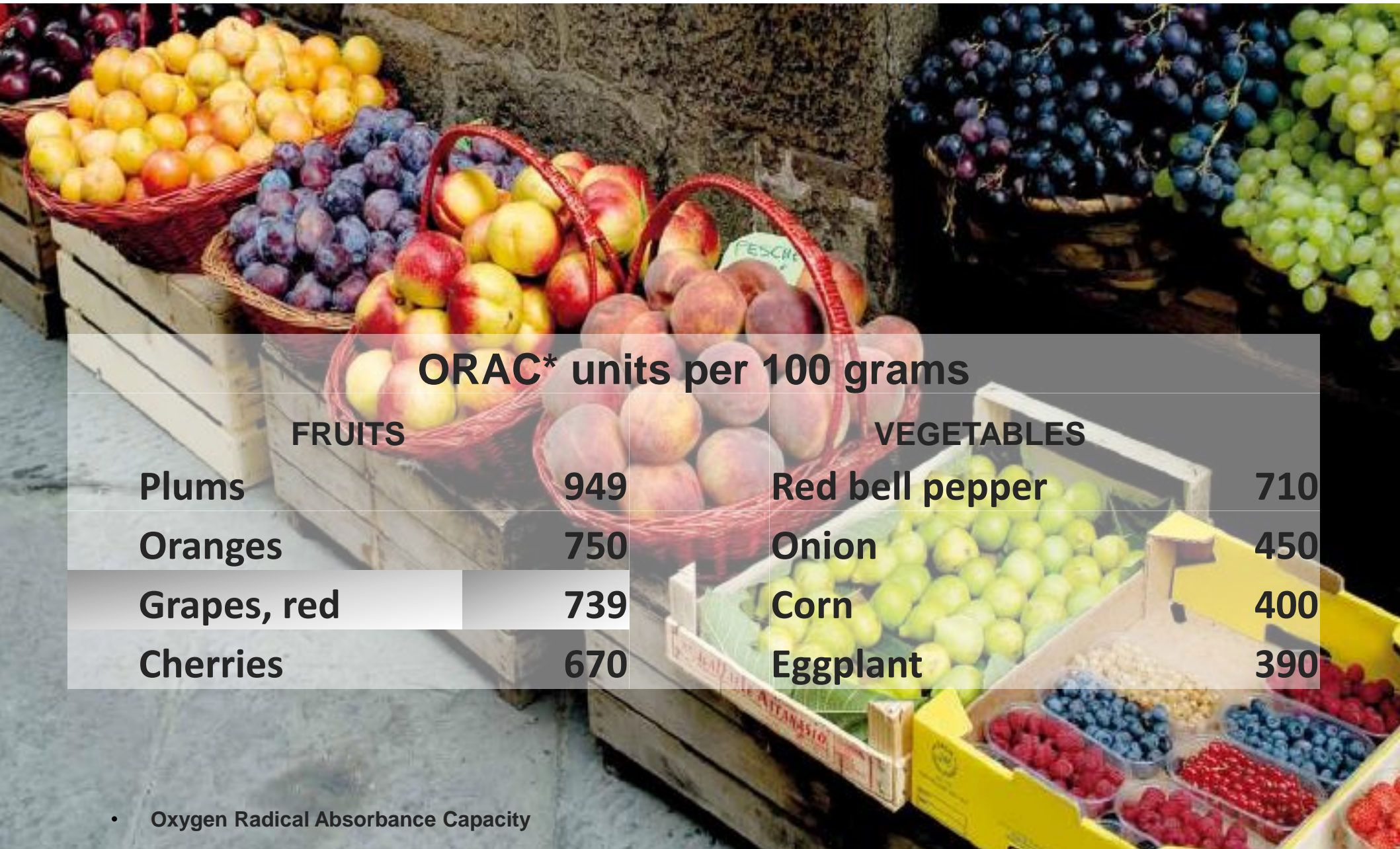
Any type of solid formulations

pH<5 for liquid formulations



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# TOP ANTIOXIDANT FOODS



## ORAC\* units per 100 grams

### FRUITS

Plums	949
Oranges	750
Grapes, red	739
Cherries	670

### VEGETABLES

Red bell pepper	710
Onion	450
Corn	400
Eggplant	390

- Oxygen Radical Absorbance Capacity



# Water Footprint

1 gram	Water footprint (L/gr)	ORAC per gr	ORAC/ L of water consumed
Grape	2.4	7.4	3
Echinacoside HTN	1.4	2800	2030

