



Peptidyss

for stress management



May 2020





French Biotech Expertise in Research, Science
and Innovation

Natural health solution from marine
bioresources

Our mission is to improve human health and well
being with sustainable natural products with
scientifically based data



Our healthy-aging platforms



Cognition

Memory boost
Sleeping disorders
Stress management



Mobility

Joint care
Bone health
Muscle recovery



Beauty

Skin beauty
Slimming
Nails and hair



When our ancestors were using biotechnology

Our ancestors already used marine resources in feeding and medicine

Indeed, historians found traces of Garum, a fermented fish sauce very appreciated in the Roman Empire for its positive effects on health and well-being.

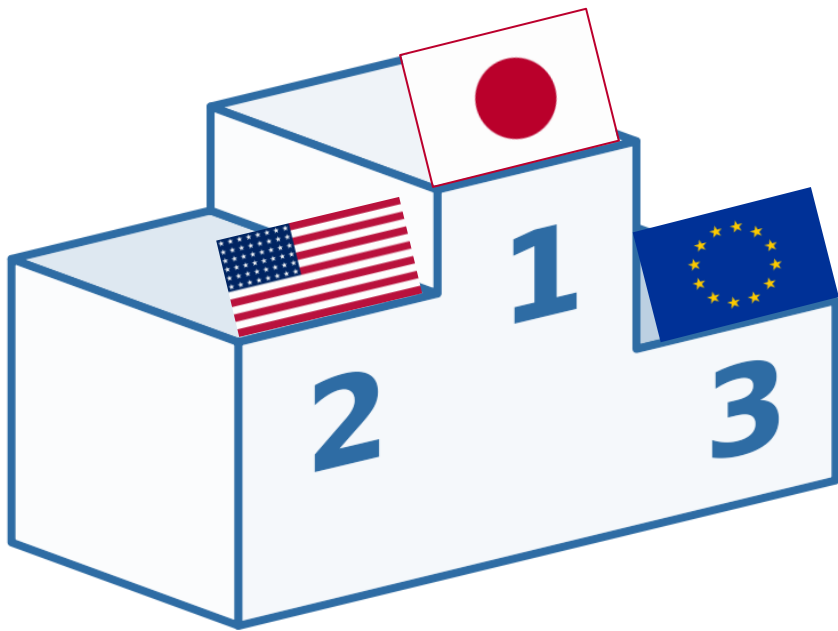
Perhaps this is the reason why in the famous comics “Asterix and the great crossing”, Getafix (Panoramix), who is out of fresh fish to make the magic potion, asks Asterix to go fishing...

When History inspires fiction !

Archeologists discovered Garum production sites all over the Atlantic facade but the biggest was found in Douarnenez, south Finistere, Brittany (France).



Stress in figures



The global stress management supplement market is expected to grow

- ⇒ Japan is the most stressed country worldwide with about 60% people declaring they are stressed¹
- ⇒ In 2017, USA represented around 34% of the global stress management supplement market
- ⇒ Europe (Iceland, Portugal, Denmark, Sweden, the UK...) has the highest demand for stress management and antidepressant supplements

European market top 3 countries where people are the most stressed in everyday life:

1. Poland (25%)
2. Germany (20%)
3. France (19%)

On French market, stress management and sleeping disorders are both among the top 3 of the nutraceutical market²

22% of people take dietary supplements because of stress issue (based on people who have already consumed dietary supplements before)³

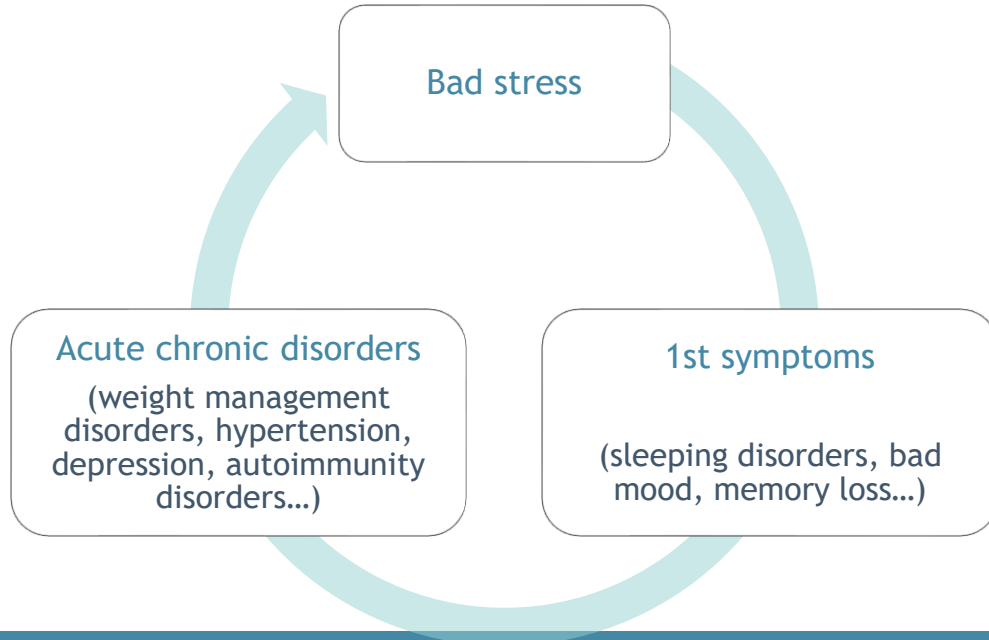
What is stress?

A natural phenomenon

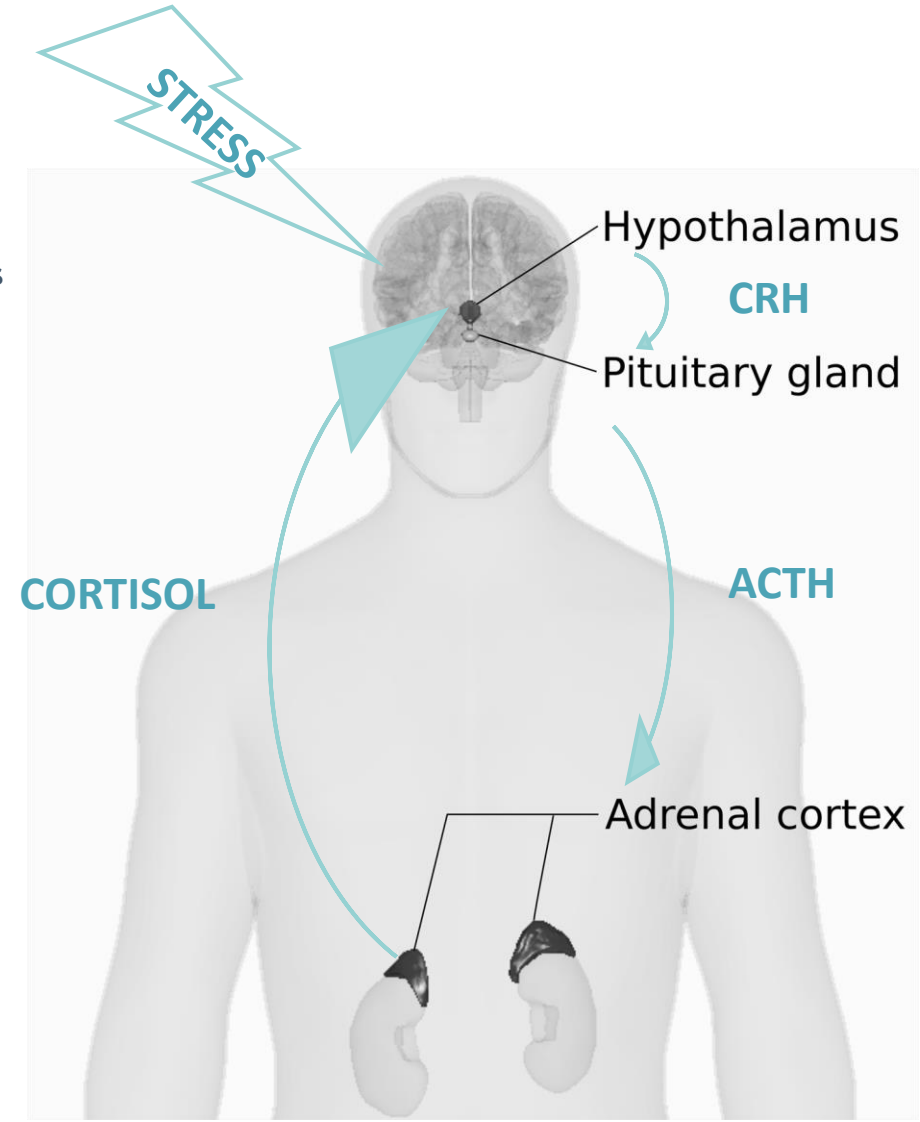
Our body adapts punctual situations of pressure with a natural physiological reaction called **stress response**

Good stress vs. bad stress

Positive stress, **punctual** → adrenalin, good energy



THE solution?
Natural bioactive peptides



Stress management strategies

- Cognitive behavioral therapy
- Relaxation
 - Not always enough if stress and its symptoms become harmful.

Non-pharmacological approaches



- Anxiolytics
 - Known risks of adverse effects and dependency
 - Generally indicated for more severe situations

Pharmacological treatments



- Plants³
- Food hydrolysates with Anxiolytic-like peptides^{4,5}
 - Fewer adverse effects
 - Lower risk of dependency
 - Good bioavailability

Dietary supplements



3 – Sarris J *et al.*, *CNS Drugs*, 2013

4 - Liu & Udenigwe, *J. of Food Biochem.*, 2019

5 - Zamora-Sillero *et al.*, *Marine Biotechnology*, 2018

Peptidyss® : efficient for stress management

Specific unique composition based on sardine protein hydrolysate

Composition	Peptidyss® (in %)
Total proteins (N*6,25)	≥ 70
Minerals	≤ 20
Lipids	≤ 2

A natural and sustainable marine ingredient

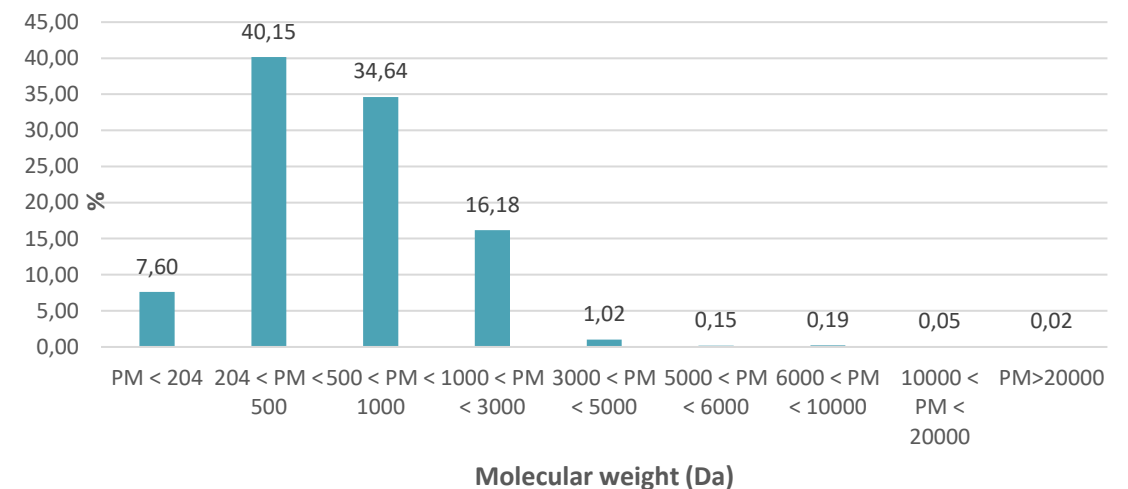
Peptidyss® is made from by-products collected in local fishing industries.

Its process is totally clean and respects the environment.

High digestibility, high biodisponibility

Made of 98% of peptides with a molecular weight <3000 Da, Peptidyss® is highly digestible and bioavailable.

Peptide molecular weight repartition

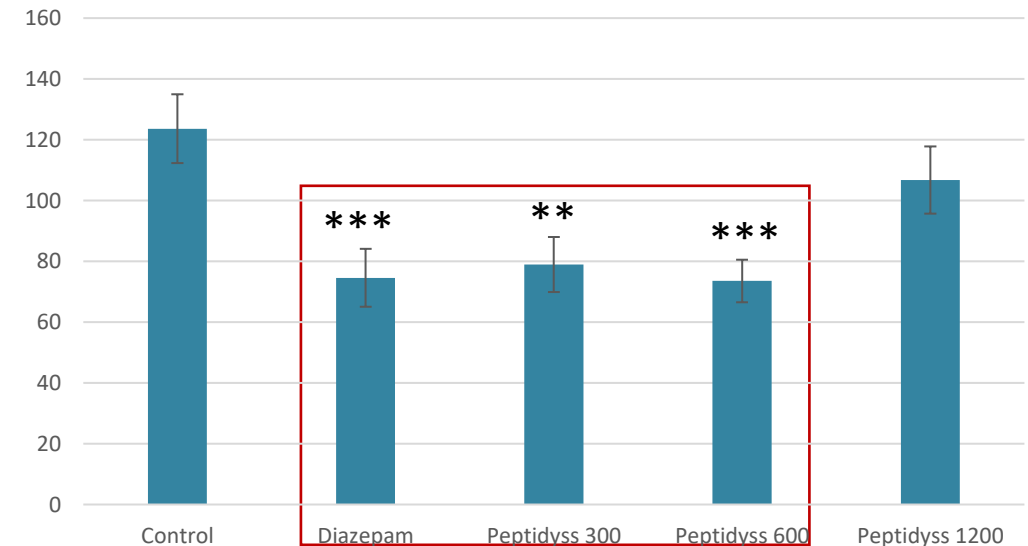


Several toxicity testings have been conducted and demonstrated Peptidyss® safety even with high dosage

Study #1: Anxiolytic-like effects of Peptidyss®

- **Defensive burying test** on male Wistar rats based on the rodents' trend to bury the source of a noxious stimulus (shock-probe).
- **5 groups** (n =12) with an oral administration 60 min before the test:
 - Control: 1% methylcellulose solution 5 mL.kg⁻¹
 - Diazepam: 3 mg.kg⁻¹
 - Peptidyss® : 300, 600 and 1200 mg.kg⁻¹
- **Anxiety global score** calculated thanks to recorded variables:
 - Duration of probe-burying,
 - % of approaches towards the probe followed by retreats

Effects of Peptidyss on the anxiety global score



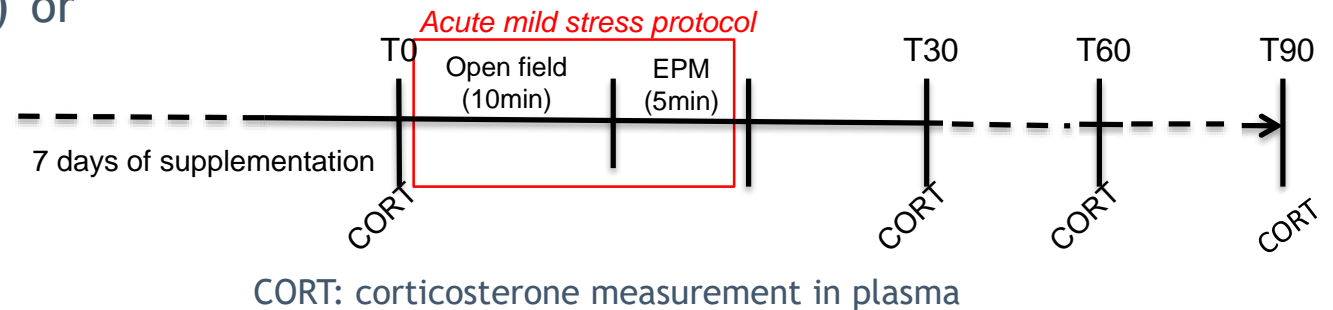
Significant anti-stress activity of Peptidyss® 300/600 mg/kg
Diazepam-like effects of Peptidyss® 300/600 mg/kg with no adverse effects

Study #2: Anti-stress effects of Peptidyss®

Evaluation of Peptidyss® supplementation on stress reactivity in mice, in a situation of moderate acute stress (a stress of everyday life)

4 groups (n =13) with daily supplementation by oral feeding of water (control group) or Peptidyss® 300 mg. Kg⁻¹:

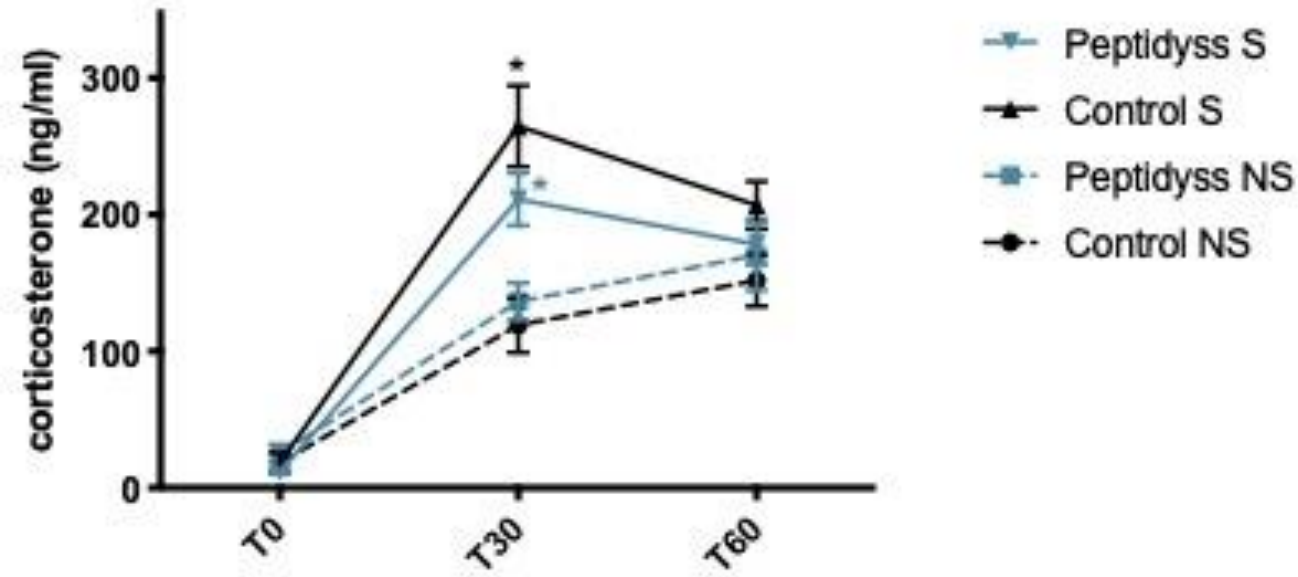
- Control No Stress (NS)
- Control Stress (S)
- Peptidyss® NS
- Peptidyss® S



Dinel *et al*, in preparation

* EPM : Elevated Plus Maze

Study #2: Anti-stress effects of Peptidyss[®]



✓ Peptidyss[®] supplementation significantly modulates the peak of corticosterone secretion 30 min after an acute moderate stress.

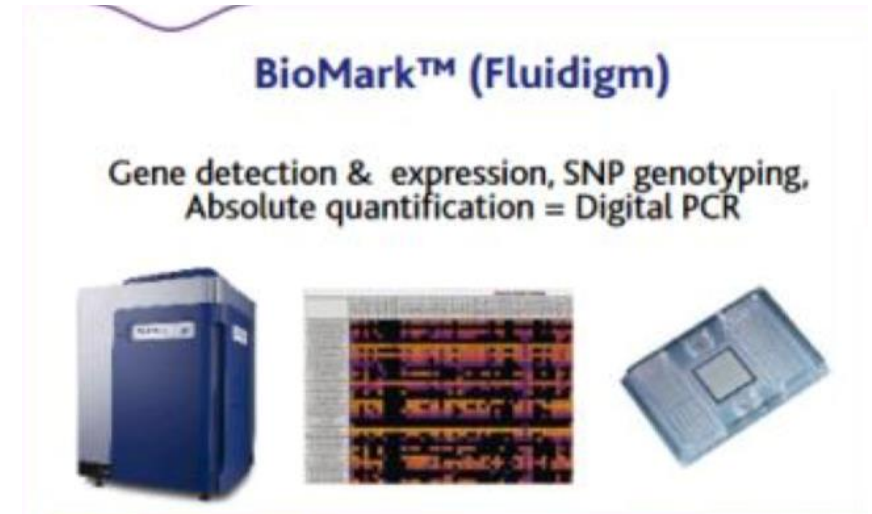


Peptidyss[®] supplementation could help to prevent deleterious effects induced by an exacerbated (dysregulated) corticosterone secretion.

Dinel *et al*, in preparation

Study #2: Understanding the mechanisms implicated in effects induced by Peptidyss[®] supplementation

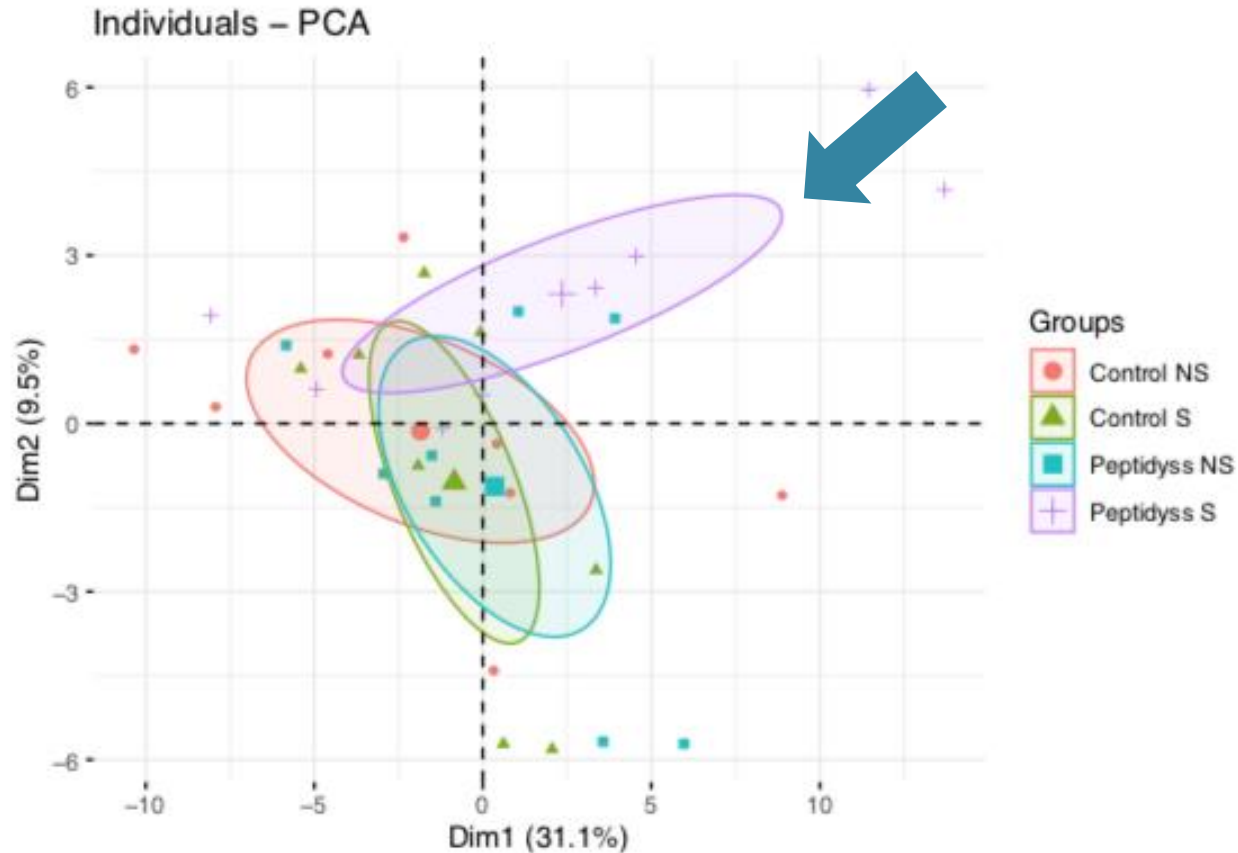
- Evaluation of **gene expression in hippocampus**, (structure highly involved in memory and stress): 4 groups, n = 8.
- Focus on **stress system, circadian rhythm, neuronal structure, cellular communication, oxidative stress: 93 stress-responsive genes selected**^{7, 8}.



Dinel *et al.*, in preparation

Study #2: Peptidyss® effect on modulation of stress-responsive gene expression

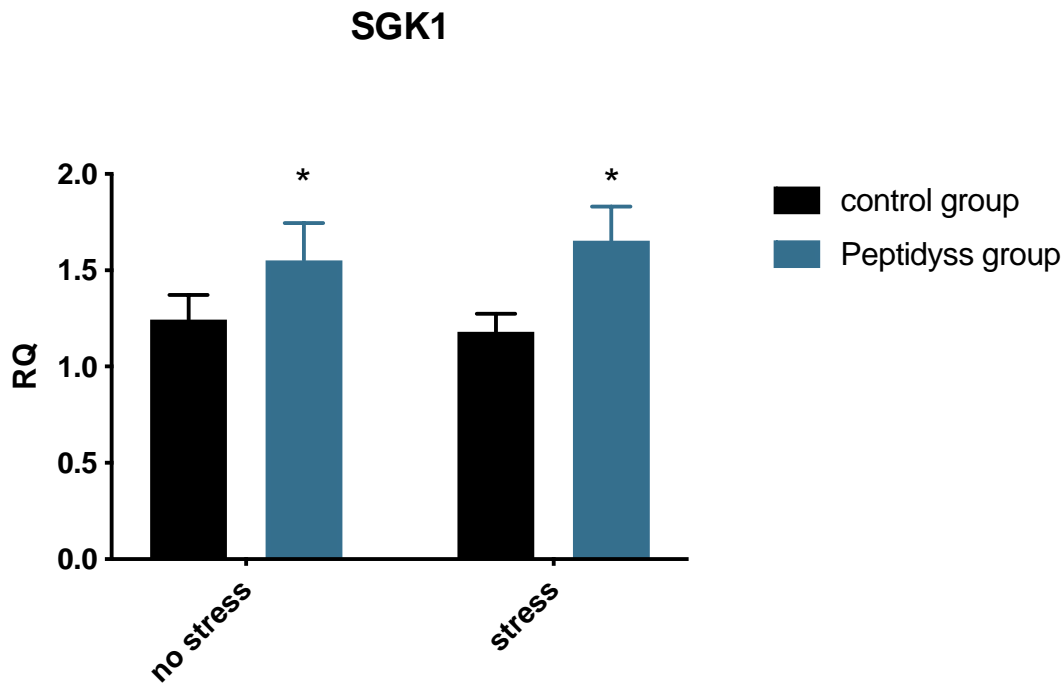
PCA of genes evaluated in hippocampus



After a moderate acute stress, Peptidyss® supplementation induces a modulation of the pattern of stress-responsive genes expression compared to other groups

Dinel *et al*, in preparation

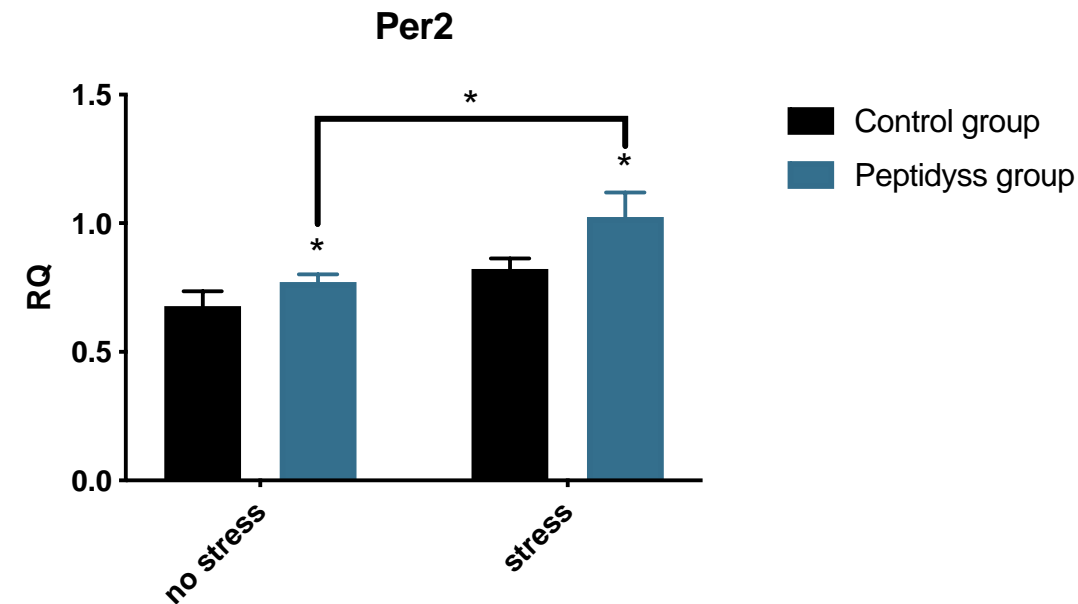
Study #2: Peptidyss[®] supplementation induces a modulation of expression of gene implicated in stress pathway



- ✓ The serum- and glucocorticoid-inducible kinase 1 (SGK1) is a serine/threonine kinase implicated in the cellular stress response and neuronal function.
- ✓ SGK1 has been identified as a mediator for the effects of cortisol on neurogenesis and glucocorticoid receptor function, with particular relevance to stress and depression⁹.
- ✓ SGK1 is upregulated by the Peptidyss[®] supplementation.

Dinel *et al*, in preparation

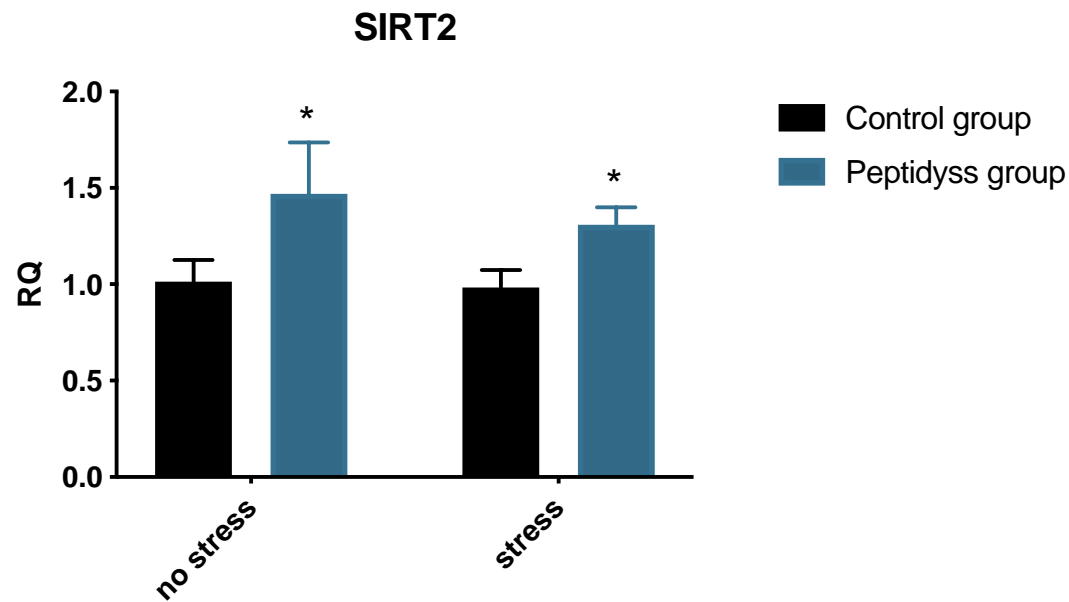
Study #2: Peptidyss[®] supplementation induces a modulation of expression of gene implicated in circadian rhythm



- ✓ The period circadian clock 2 (Per2) gene, a gene classically described as one of the most important circadian rhythm gene¹⁰ is modulated by stress.
- ✓ Per2 is upregulated in stressed animals supplemented with Peptidyss[®] compared to stressed animals supplemented with saline.

Dinel *et al*, in preparation

Study #2: Peptidyss[®] supplementation induces a modulation of expression of gene implicated in aging process



- ✓ Sirtuin 2 (SIRT2) plays diverse roles in cellular metabolism and especially for aging process.
- ✓ Several studies¹¹ show that SIRT2 acts as a powerful regulator of aging with a potential role in neurodegeneration.
- ✓ SIRT2, is upregulated by Peptidyss[®] supplementation.

Dinel *et al.*, in preparation

Going further on bioactive peptides research

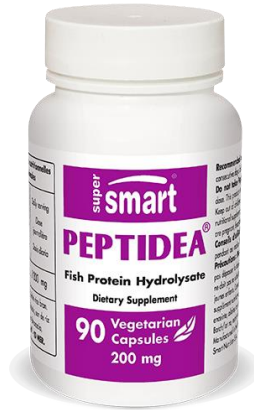


Collaborative research program supported by EU (FEDER) and Region Bretagne (2018 - 2021)

- Upgrade of our **Stress Management Solution Peptidyss®** by developing new generation of unique ingredients based on **premium marine bioactive peptides**
 - Peptidyss® knowledge
 - Peptidyss® anxiolytic-like and anti-stress effects demonstrated by pre-clinical studies
- Identification, from marine bioresources, of **specific bioactive peptides** with stress management properties
 - Expertise in **Peptidomics / Bioinformatics** and **efficacy tests**
- Launching of a new ingredient from VIPP project by the end of 2021
 - Expertise in **micro encapsulation** and **hydrolysis process**
- Opening to new health applications
 - e.g. sleeping disorder

Peptidyss® : dosage & how to communicate

Example of products with Peptidyss®



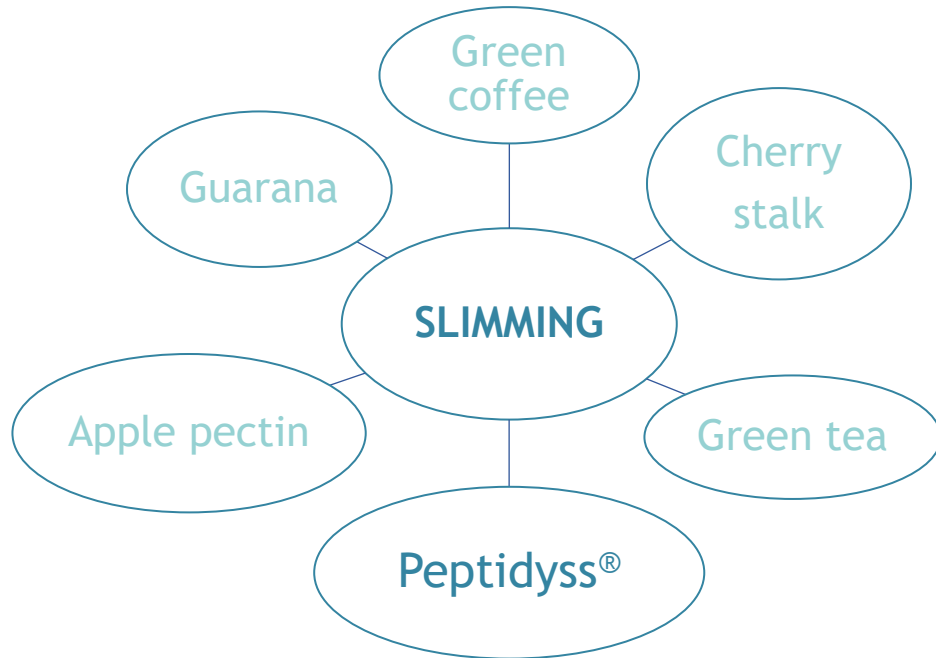
Peptidyss® daily dosage:
500 mg to 1400 mg

How to communicate?
Peptidyss® and/or Magnesium
and/or Vit B and/or plants

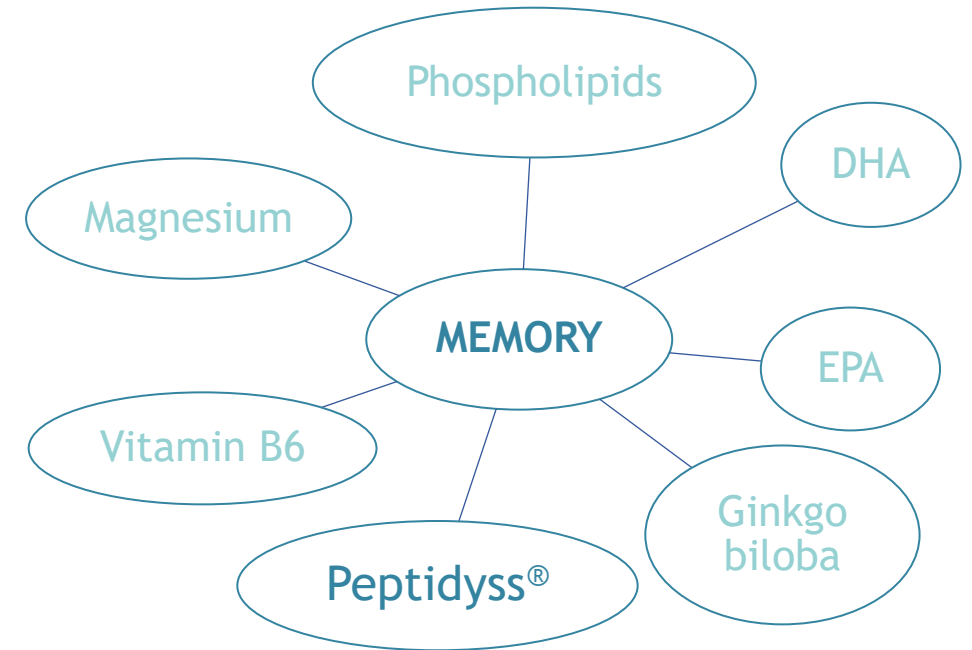
Formulation tips:
Yellowish powder with a specific
test and odour
Dry or liquid forms (powder,
stick, tablet, capsule, soft gels,
need to be shaken)

Conditions:
dry environment, low ambient T°

Peptidyss[®] : some ideas about formulation

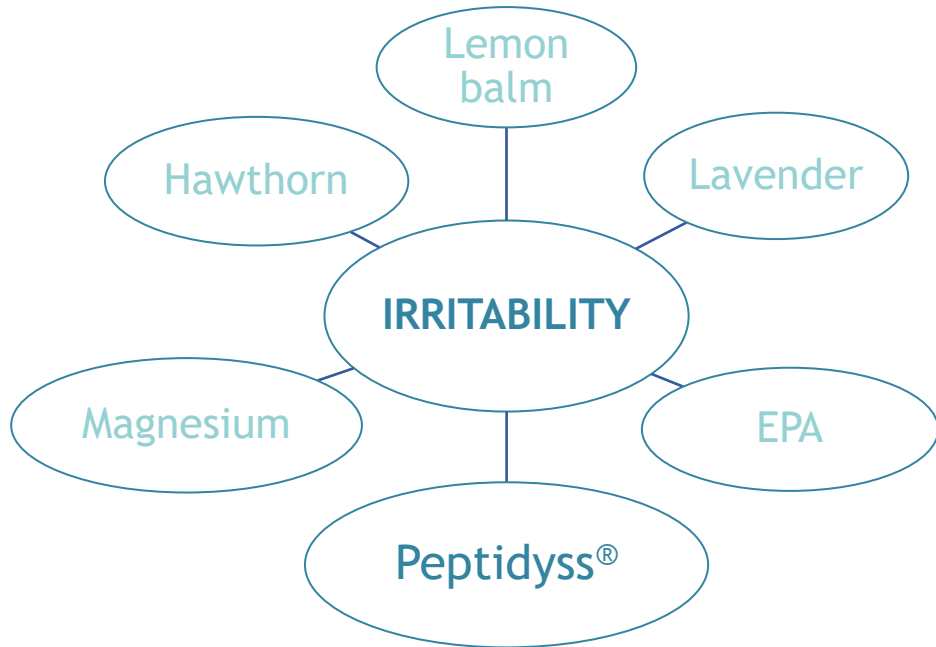


Peptidyss[®] incorporated into slimming formulations will help to manage stress and to avoid temptations.

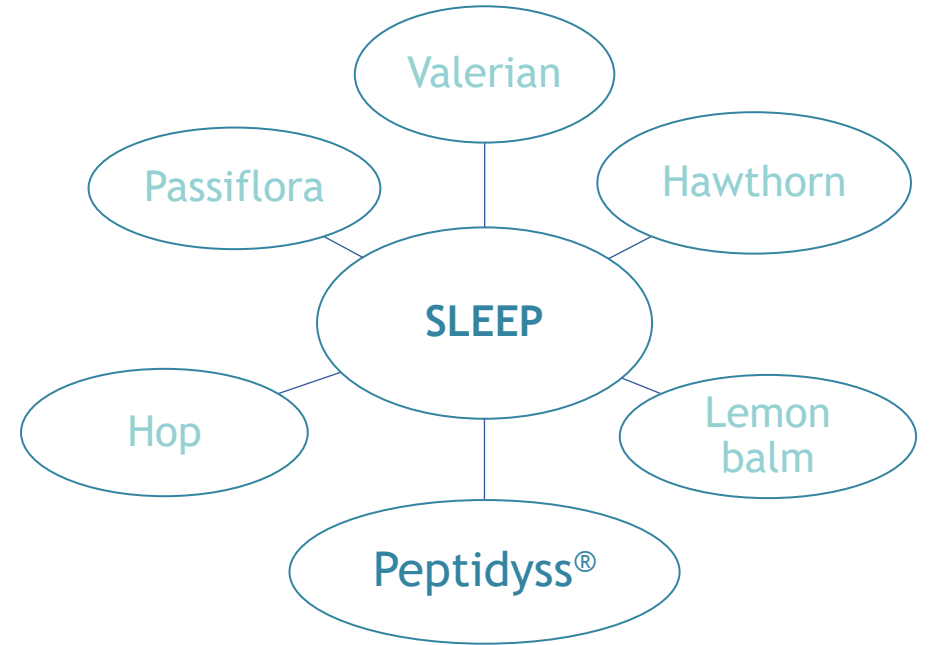


Peptidyss[®] allows to reduce stress-related negative effects and to diminish temporary memory troubles.

Peptidyss[®] : some ideas about formulation

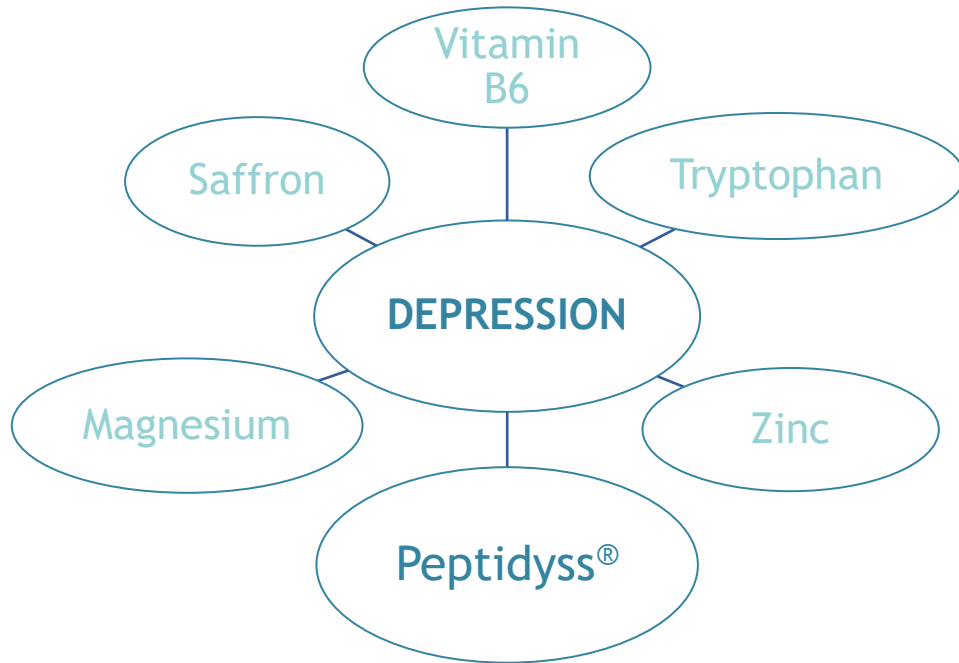


Irritability and anxiety are often related to stressful periods. Peptidyss[®] helps regulating stress and diminishing irritability.

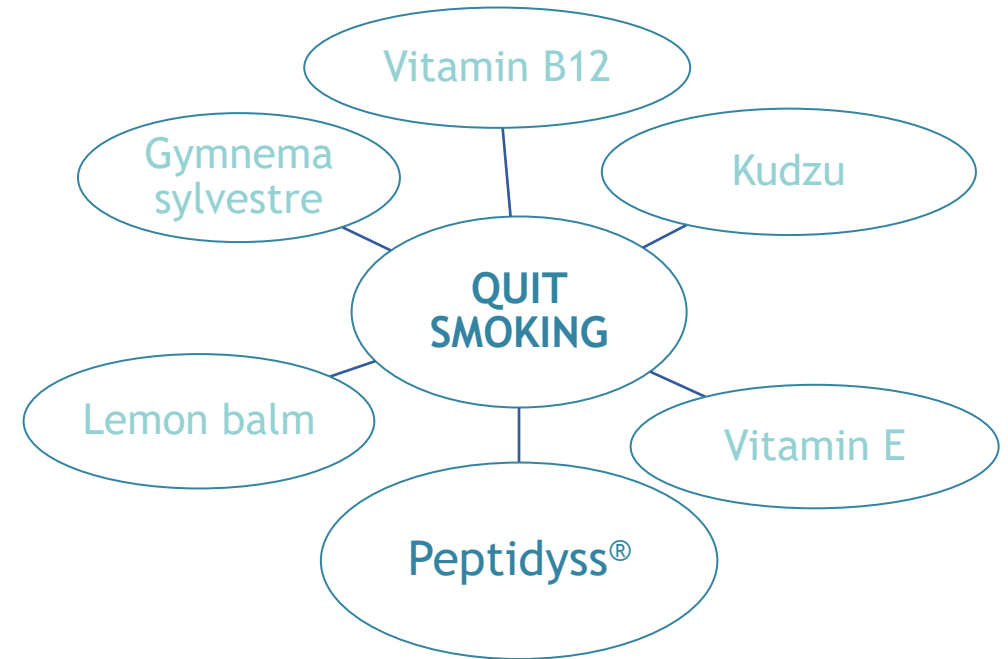


Stress may cause sleeping disorders. Peptidyss[®] improves your sleep at night.

Peptidyss[®] : some ideas about formulation



General unhappiness and depression may be caused by stress. Peptidyss[®] has an effect on the body helping to manage stress.



Stress may reduce the chances of quit smoking and makes us fall back into habits. Peptidyss[®] reduces stress-related effects diminishing desire to smoke.

Peptidyss[®] : a response to consumer expectations

✓ Scientific based product

- 2 pre-clinical studies:
- Diazepam-like effects of Peptidyss[®] 300/600 mg/kg with no adverse effects
 - Regulation of the corticosterone secretion in moderate acute stress

Investigation of the underlying mechanisms: publication pending

Ongoing scientific research regarding the identification and characterisation of bioactive peptides (VIPP project)

✓ Natural & eco-friendly

Peptidyss[®] is made from **marine by-products*** with a process using a natural enzyme (hydrolyse = water extraction) with no chemicals or preservative.

Valuation of fish by-products → added-value, « blue ecology » and sustainability

✓ Cost competitive

* Usual wasted part of the fish is 50% to 75% of the fish weight

Any question ?



*Our team remains at your service
for further information*

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- Market source : The Workforce View in Europe 2019, ADP, Mars 2019
- Market source : « 6 New stress statistics from around the world », The Busy Life
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