**Pr. Jacques Fantini**
**Professor of Biochemistry – Aix Marseille University**

**د. جاك فانتيني**
**أستاذ الكيمياء الحيوية – جامعة ايكس مارسيليا**

# Broad antiviral activity of *Nigella sativa*. A unique mechanism of action ?

Pr. Jacques FANTINI, University of Aix-Marseille France

*Rational Healthy Food & Herbal Contributing to Sustainable Development Goals Conference*

# On a global perspective, we need a rational, complete, and widely accepted theory to explain phytotherapy efficacy and the mechanisms of action in herbal drugs

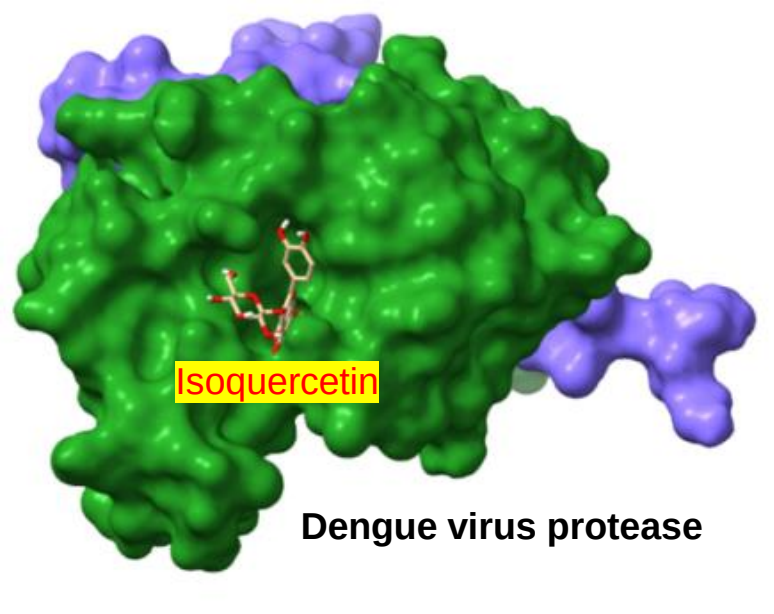
*Commentary*

**Pharmacological Activities of Phytomedicines: A Challenge Horizon for Rational Knowledge**

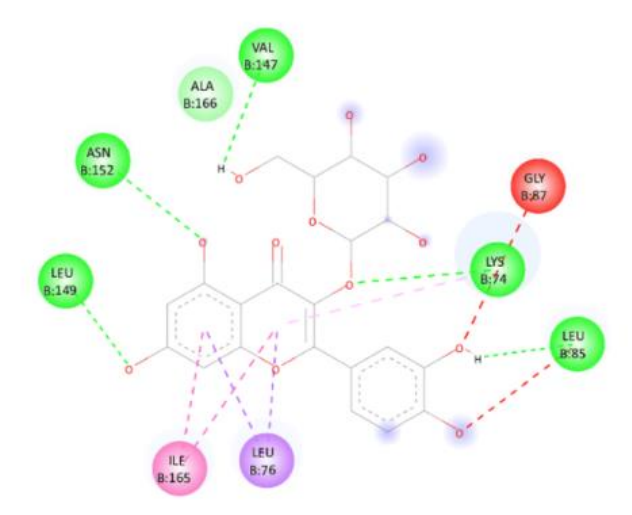
Javier Rodríguez Villanueva [1,*], Jorge Martín Esteban [2] and Laura Rodríguez Villanueva [2]

## *N. sativa* : broad antiviral activity
## What about its mechanism(s) of action ?

# Binding of phytochemicals from *N. sativa* to virus proteins




Dengue virus protease



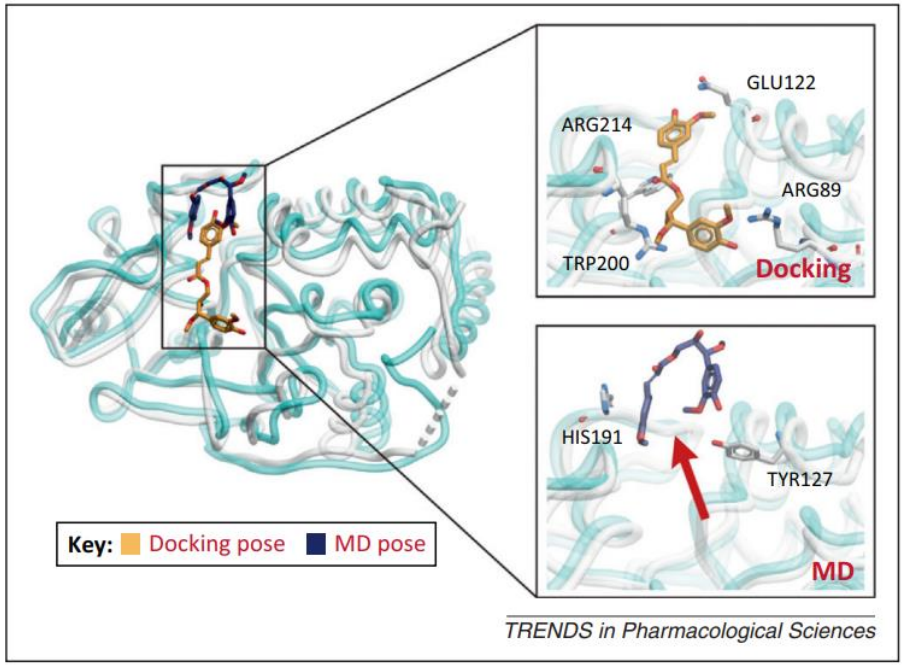

Ligand binding pocket

# Several compounds, different docking

| Ligand | Receptor proteins | Binding energies (kcal $mol^{-1}$) | Interacting amino acid residues |
|---|---|---|---|
| Apigenin | NS5 | −9.9 | Leu94, Ile72, Pro298, Lys355, Val66, Gln351 |
| Astragalin | NS5 | −8.5 | Thr51, Ile691, Asp690, His52, Gln693, Val687, Ala259 |
| β-Sitosterol | NS5 | −8.0 | His52, Ile691, Ala535, Val687, Ala259, Tyr119 |
| Campesterol | NS5 | −8.5 | Tyr119, Ala535, His52, Val687, Ala259, Pro363, Tyr119 |
| Carvone | NS5 | −6.4 | Pro298, Val66, Ile72, Arg581, Pro582 |
| Cycloeucalenol | NS5 | −8.0 | Val603, Phe485, Ile797, Tyr606, Asp663 |
| Dithymoquinone | NS5 | −7.5 | Val687, His52, Pro692 |
| D-Limonene | NS5 | −6.0 | Pro298, Val66, Lys95, Pro73, Leu94, Ile72 |
| Isoquercetin | NS5 | −8.6 | His52, Thr51, Ile691, Asp690, Gln693, Val687, Ala259 |
| Nigellicine | NS5 | −9.1 | Arg352, Lys74, Arg352, Glu151, Val66, Leu94, Asn690, Ile165, Pro298 |
| Nigellidine | NS5 | −8.4 | Pro73, Lys96, Ile72, Leu94, Val66, Lys355, Pro298, Arg581, Glu296 |

# and so on ...

# Beware of AI !

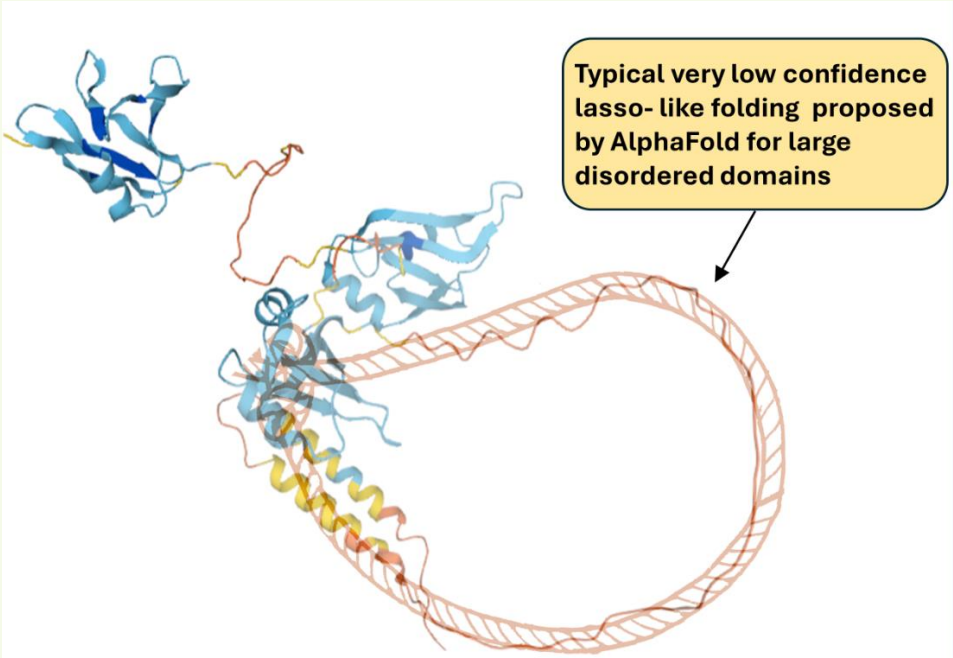



## Beware of docking!

Yu-Chian Chen[1,2,3]

Trends in Pharmacological Sciences, February 2015, Vol. 36, No. 2

# Beware of AI !




*biomolecules*

MDPI

*Article*

**The Epigenetic Dimension of Protein Structure Is an Intrinsic Weakness of the AlphaFold Program**

Fodil Azzaz, Nouara Yahi, Henri Chahinian and Jacques Fantini *

**So, let's think a little bit**

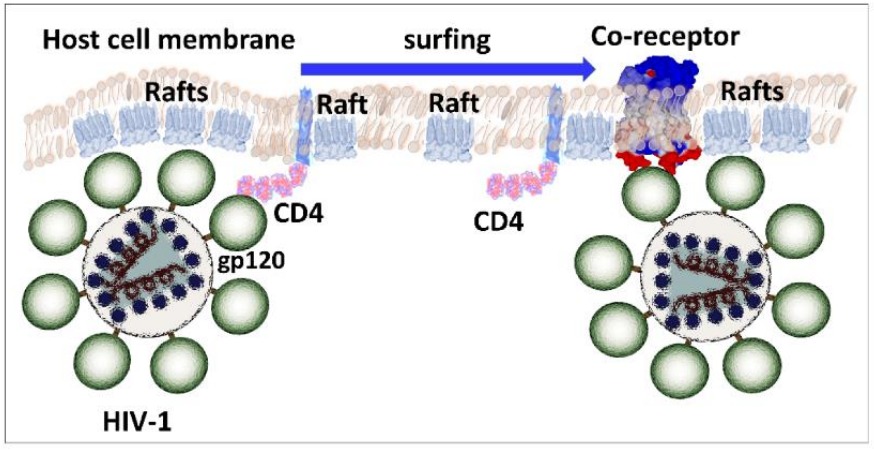
**(human touch)**

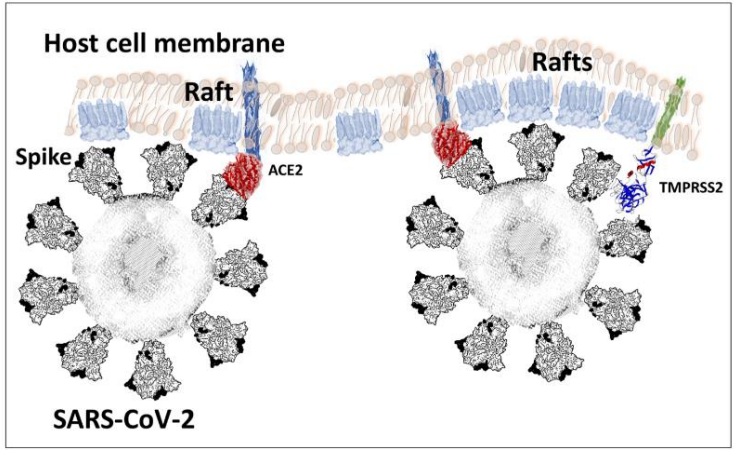
# We need a unitary mechanism

Virus

Host cell membrane

# Host cell membranes, lipid rafts and viral infection



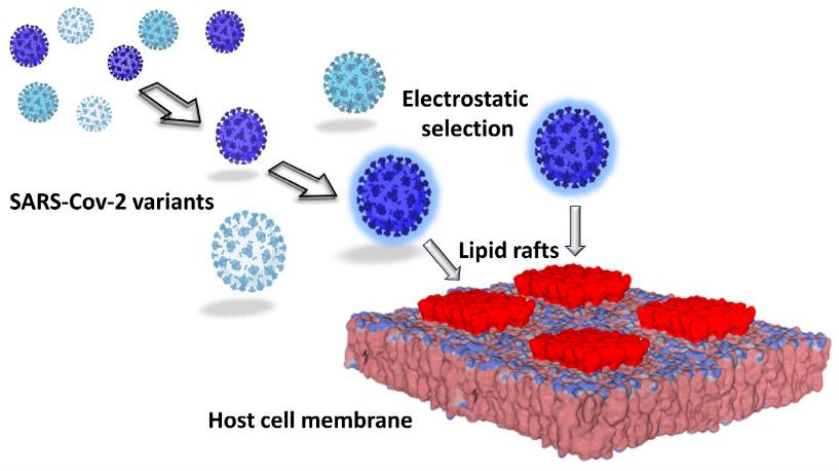



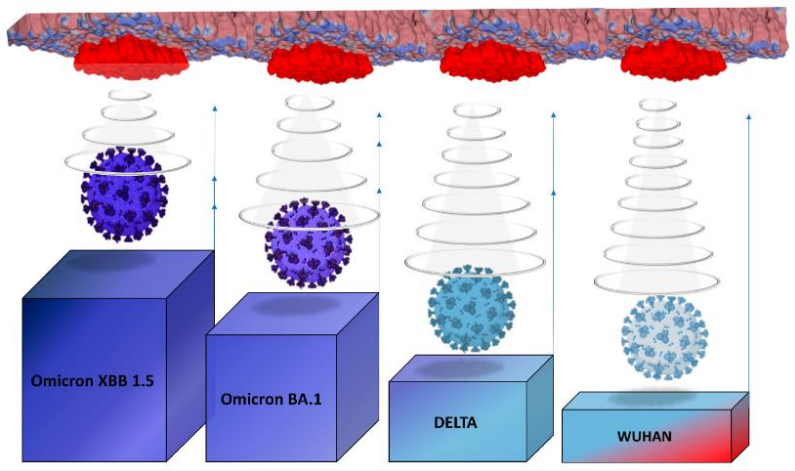

*Review*

**Convergent Evolution Dynamics of SARS-CoV-2 and HIV Surface Envelope Glycoproteins Driven by Host Cell Surface Receptors and Lipid Rafts: Lessons for the Future**

Jacques Fantini, Henri Chahinian and Nouara Yahi *

# Host membranes as drivers of virus evolution



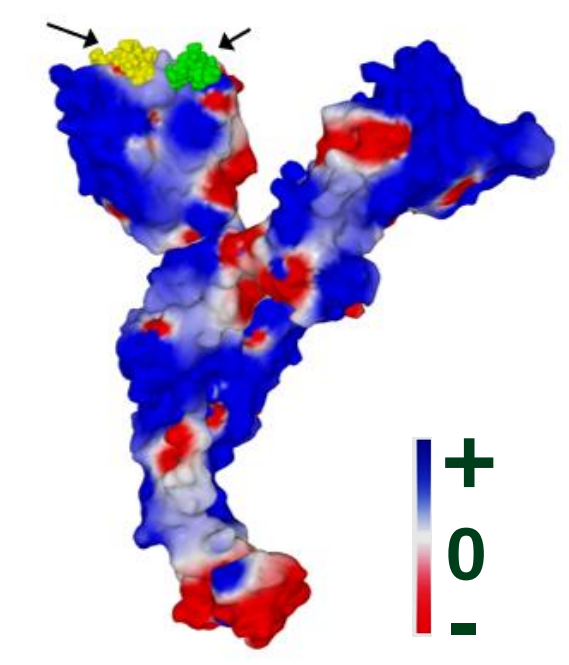

*viruses*

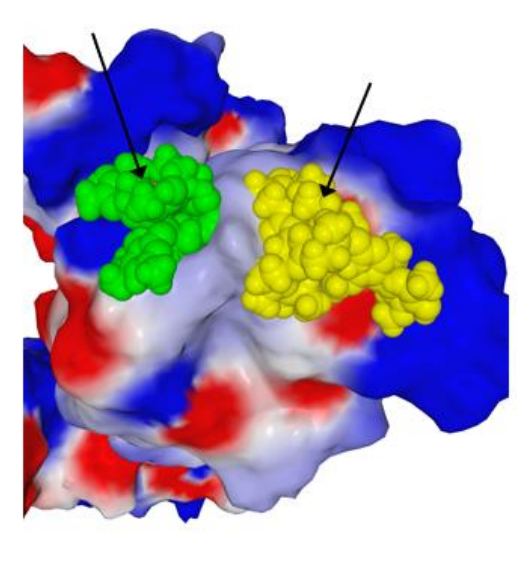
*Perspective*

**Host Membranes as Drivers of Virus Evolution**

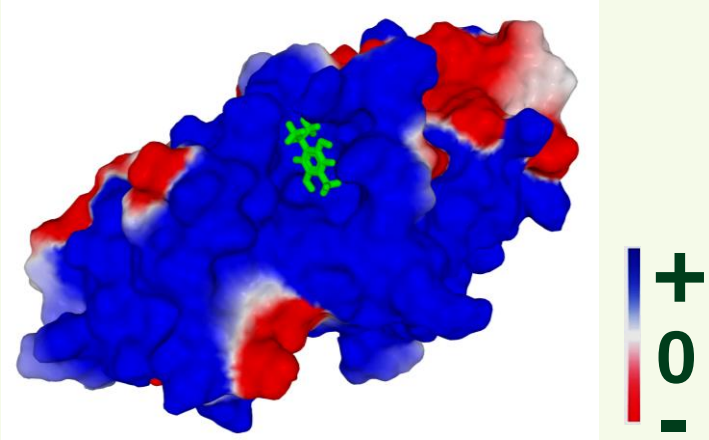
Mélanie Matveeva, Marine Lefebvre, Henri Chahinian, Nouara Yahi and Jacques Fantini *

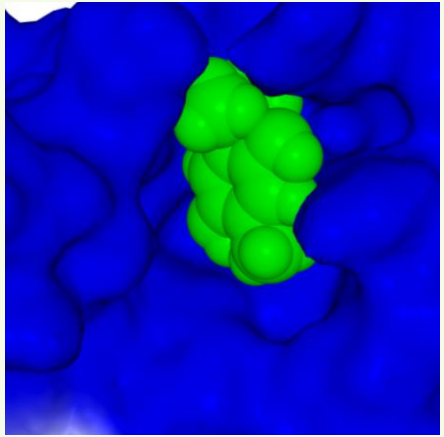
# Compound with broad antiviral activity block virus adhesion to lipid rafts



# Thymoquinone binds to virus enveloppe proteins and blocks virus adhesion to lipid rafts



# Thymoquinone, the most active antiviral phytochemical of *N. sativa*

August 30, 2019

PharmacologyOnLine

Newsletter • 2019 • vol.2 • 47-53

**A REVIEW ON ANTIVIRAL EFFECTS OF *NIGELLA SATIVA* L.**

Shamim Molla[1], Md. Abul Kalam Azad[1], Md Ali Azam Al Hasib[1], M. Monayem Hossain[1], Md. Sohel Ahammed[1], Shohel Rana[1], Muhammad Torequl Islam[1*]


**Abstract**

*Nigella sativa* seeds have wide therapeutic effects and have been reported to have significant effects against many ailments such as skin diseases, jaundice, gastrointestinal problems, anorexia, conjunctivitis, dyspepsia, rheumatism, diabetes, hypertension, intrinsic hemorrhage, paralysis, amenorrhea, anorexia, asthma, cough, bronchitis, headache, fever, influenza and eczema. Thymoquinone (TQ) is one of the most active constituent and has different beneficial properties. Focus on antimicrobial effects, different extracts of *N. sativa* as well as TQ, have a broad antimicrobial spectrum, including Gram-negative, Gram-positive bacteria, viruses, parasites, schist soma and fungi. The effectiveness of *N. sativa* seeds and TQ is variable and depends on species of target microorganisms. The present review paper tries to describe some antiviral activities of *N. sativa*. Such as murine cytomegalo virus infection, avian influenza (H9N2), Chistosoma Mansoni Infection, PPR virus, Broad bean mosaic virus, HIV virus, Hepatitis C Virus, Zucchini Yellow Mosaic Virus, and Papaya Ring Spot Virus.

**Keywords:** *Nigella sativa; antiviral effects; HIV; thymoquinone*

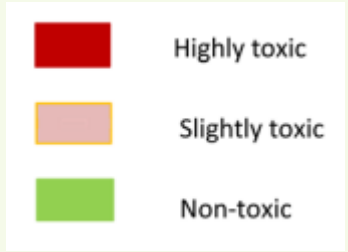
## A unique mechanism of action ?

## *Ongoing project !*

# The high therapeutic index of TQ

Predicted Toxicity risk assessment of phytoconstituents of *N. sativa*.

| Phytoconstituents | Tumorigenicity | Irritant | Reproductive Effective | Mutagenicity | Hepatotoxicity | Immunotoxicity | Cytotoxicity | Carcinogenicity |
|---|---|---|---|---|---|---|---|---|
| Apigenin | | | | | | | | |
| Astragalin | | | | | | | | |
| β-Sitosterol | | | | | | | | |
| Campesterol | | | | | | | | |
| Carvone | | | | | | | | |
| Cycloeucalenol | | | | | | | | |
| Dithymoquinone | | | | | | | | |
| D-Limonene | | | | | | | | |
| Isoquercetin | | | | | | | | |
| Nigellicine | | | | | | | | |
| Nigellidine | | | | | | | | |
| Nigellimine | | | | | | | | |
| Nigelline | | | | | | | | |
| Rutin | | | | | | | | |
| Stigmasterol | | | | | | | | |
| Taraxerol | | | | | | | | |
| Thymohydroquinone | | | | | | | | |
| Thymoquinone | | | | | | | | |



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# Thank You