The Potential of Coconut Oil and its Derivatives as Effective and Safe Antiviral Agents Against the Novel Coronavirus

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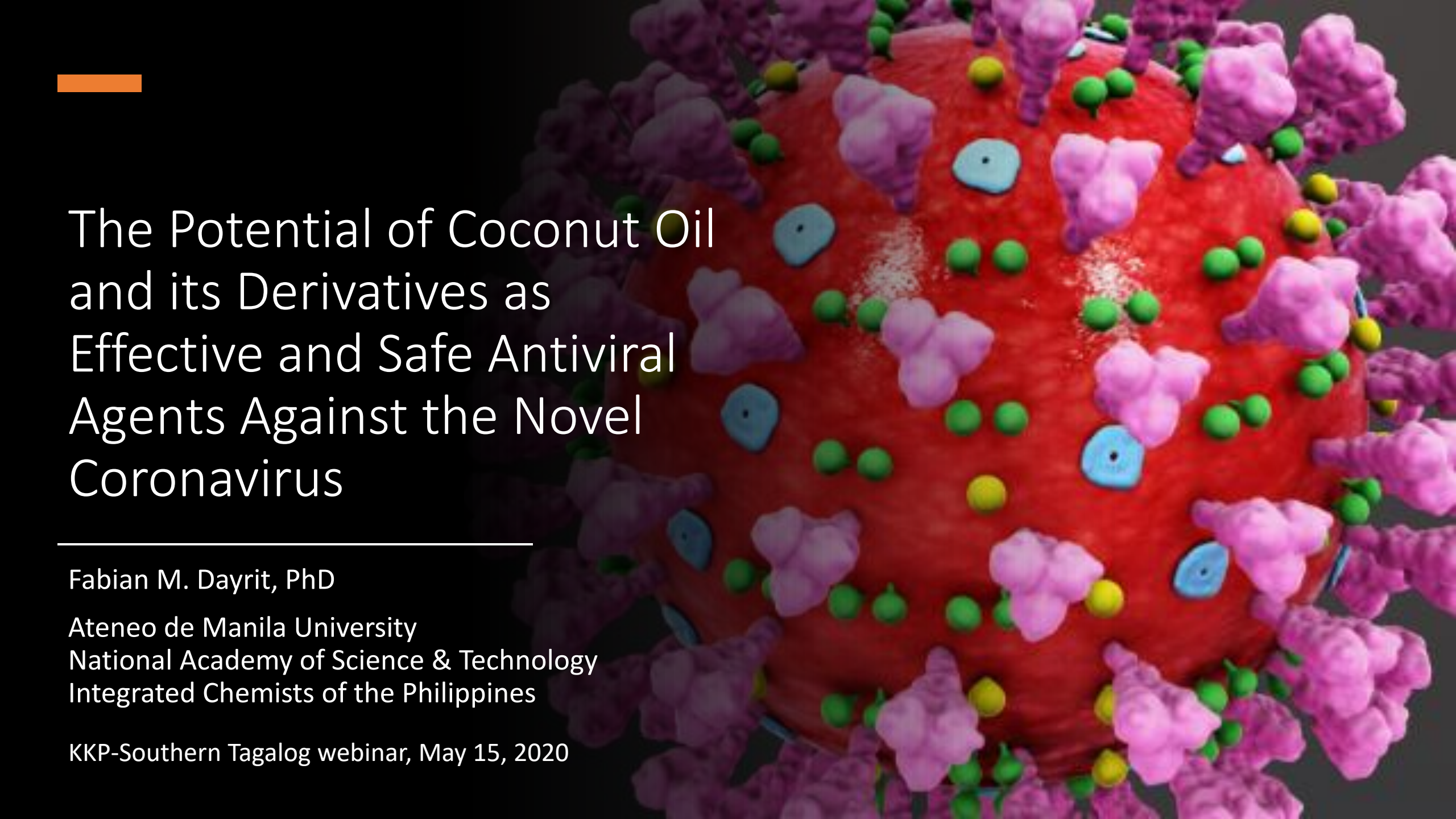
KKP-Southern Tagalog webinar, May 15, 2020



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January 31, 2020 (first version)
February 7, 2020 (second version)

As we write this, the World Health Organization has declared a global emergency over the novel coronavirus, 2019-nCoV, that has spread beyond China. There is still no cure for 2019-nCoV. 2019-nCoV has been shown to be related to SARS (Zhou *et al.*, 2020), a coronavirus which caused an outbreak in 2003. Several researchers have been designing drugs to specifically target protease enzymes in coronavirus, but testing for these drugs is many months away. What if there is a treatment candidate against the coronavirus that might already be available and whose safety is already established?

Outline

1. SARS-CoV-2
2. Coconut oil and its Antiviral Compounds
3. The Potential of Coconut Oil and its Derivatives as Effective and Safe Antiviral Agents Against the Novel Coronavirus
4. Surviving COVID-19: Go Coconuts!

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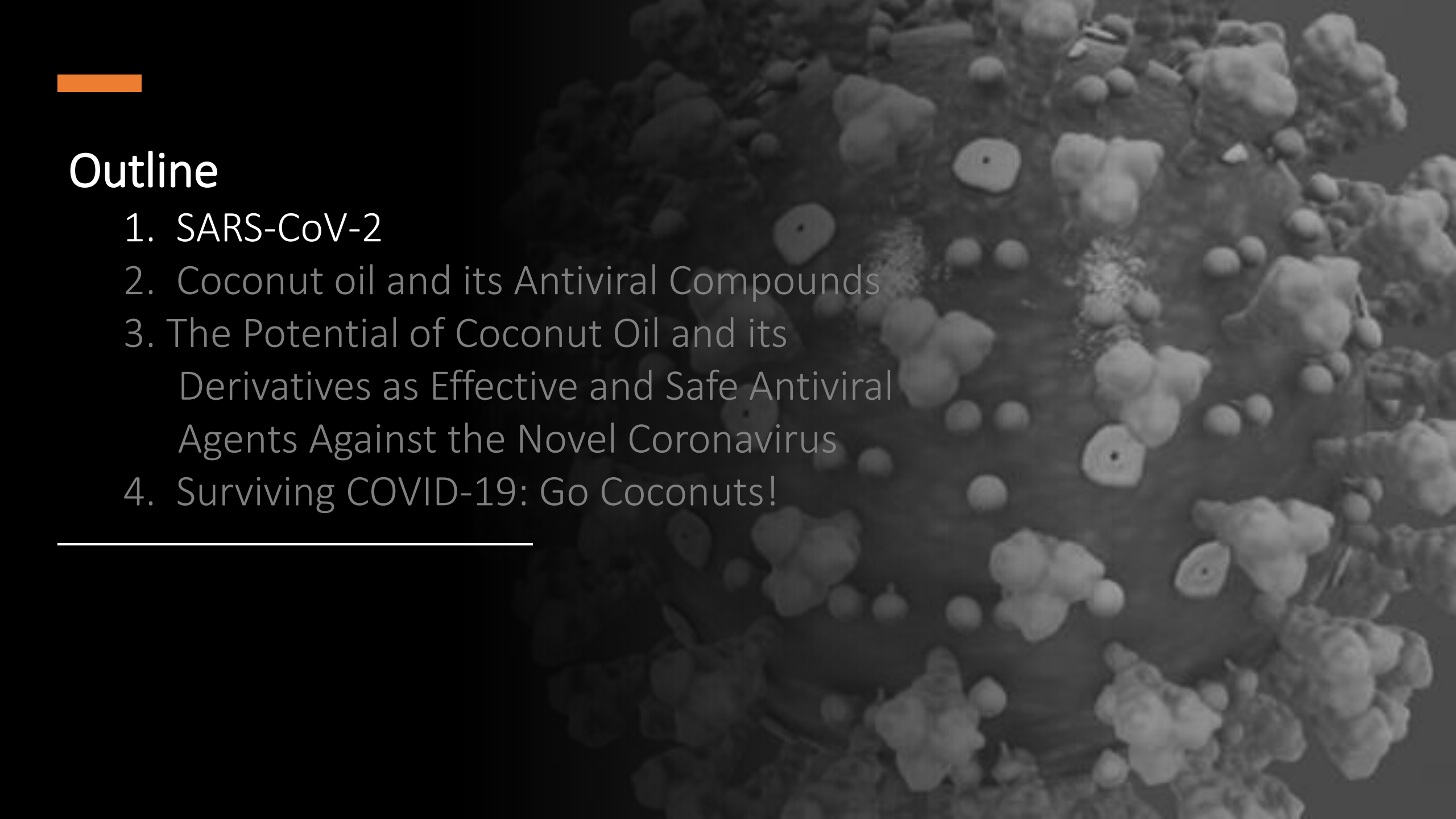
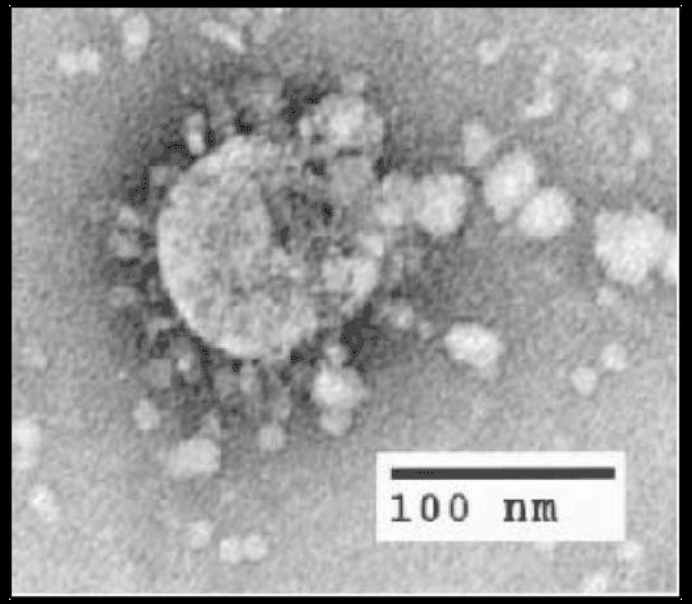
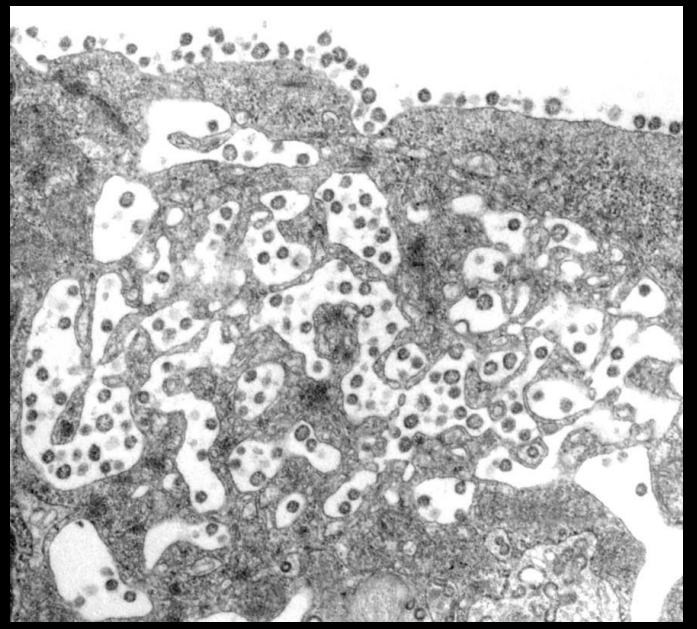


Background

- Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2, formerly called 2019-nCoV) is the strain of coronavirus that causes COVID-19. WHO declared COVID-19 a pandemic on March 11, 2020.
- There have been three recent coronavirus epidemics:
  - SARS-CoV (2002)
  - MERS-CoV (2012)
  - SARS-CoV-2 (2019)

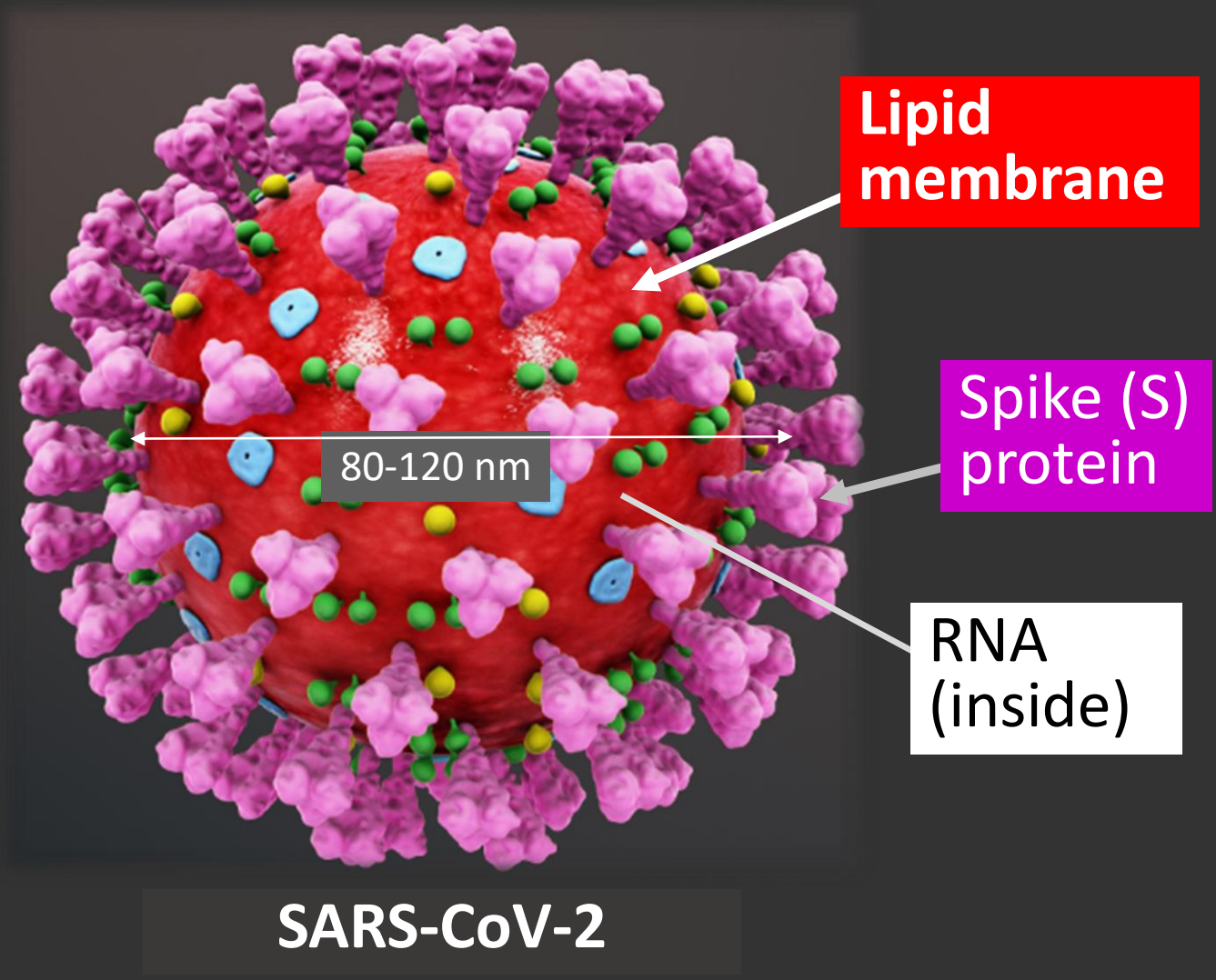


EM image of a thin section of SARS-CoV within the cytoplasm of an infected cell.
(CS Goldsmith, CDC)



A SARS-CoV-infected cell with virus particles in vesicles, migrating toward the cell surface to fuse with the plasma membrane, releasing new viral particles.
(CS Goldsmith, CDC)

- SARS-CoV-2 measures 80–120 nm (dia).
- It has four structural proteins: S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins. The S, E, and M proteins are located on the viral envelope, and the N protein holds the RNA genome inside.



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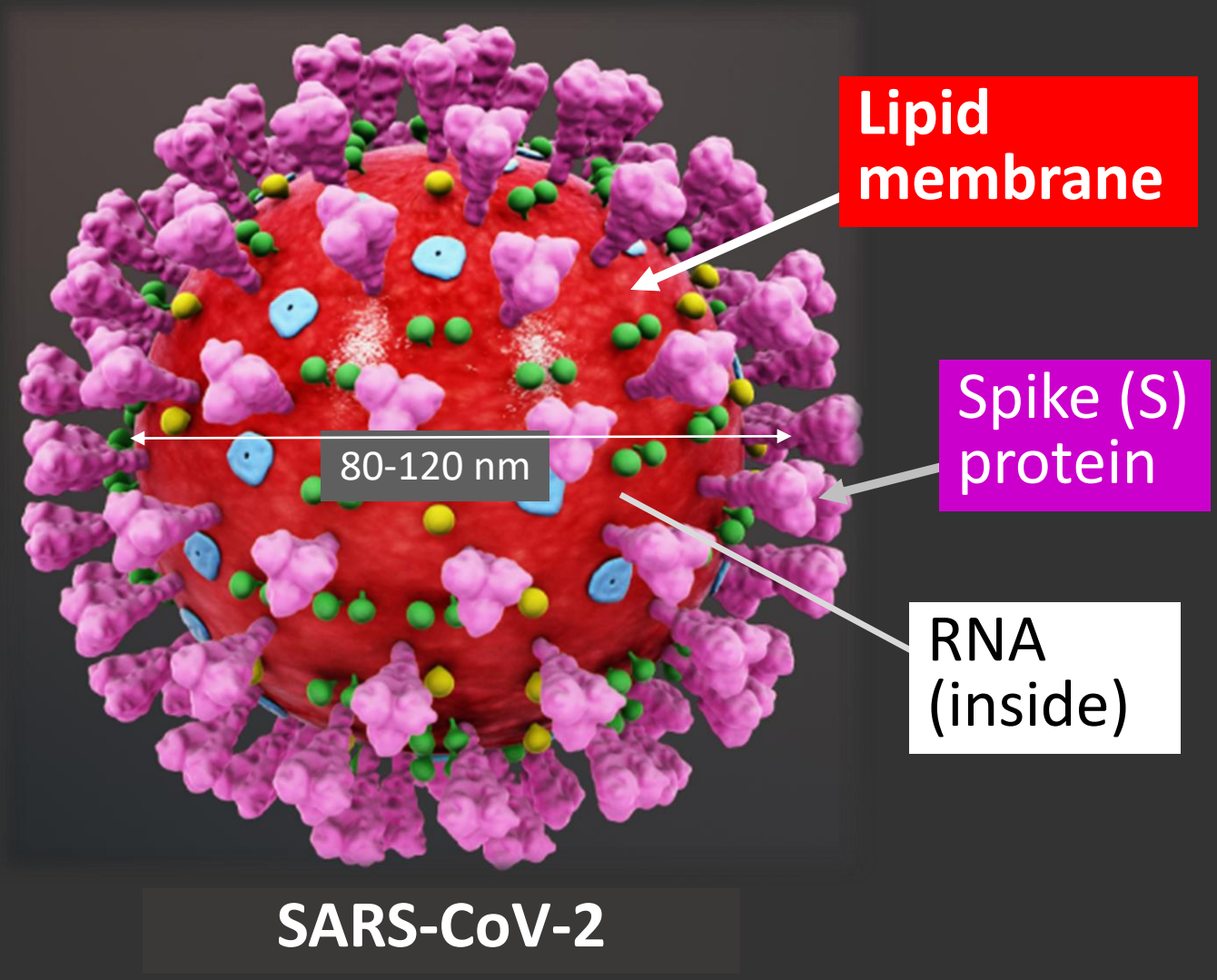
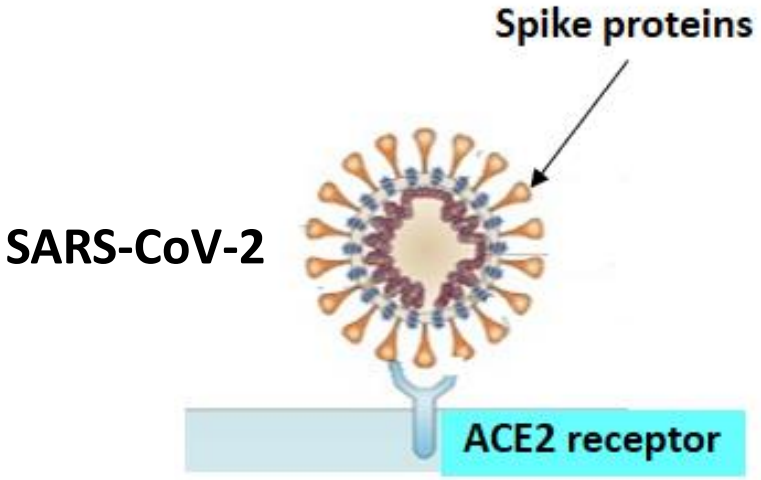
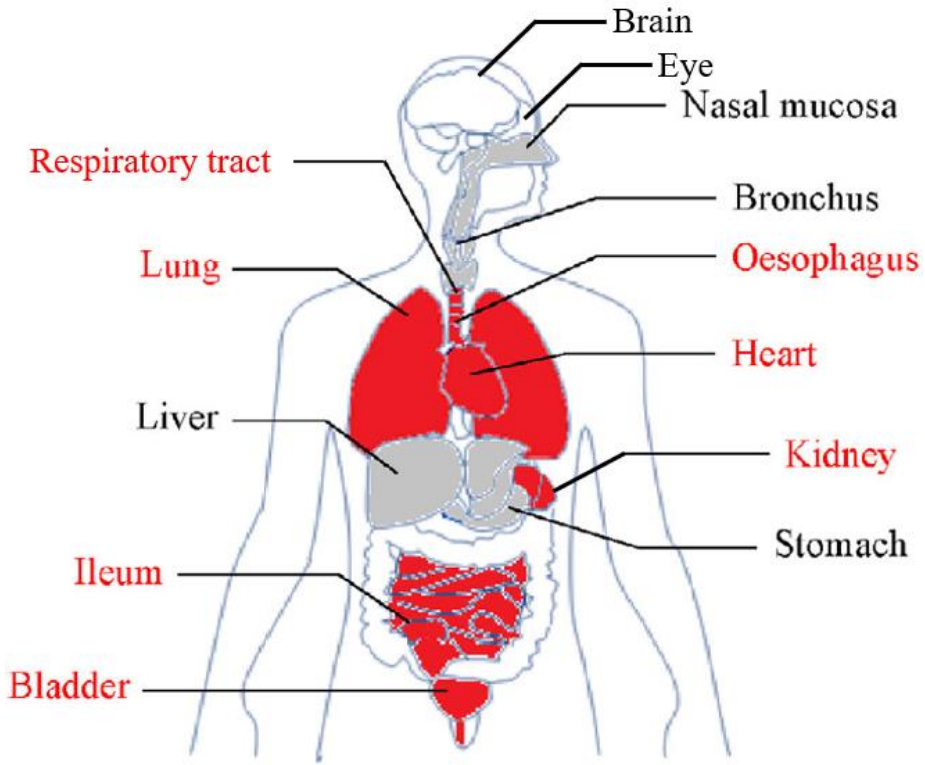
- It has four structural proteins: S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins. The S, E, and M proteins are located on the viral envelope, and the N protein holds the RNA genome inside.
- The S protein enables the virus to attach to ACE2 receptors on the membrane of the body's host cells.
- The S protein of SARS-CoV-2 has a polybasic cleavage site, which is believed to enhance cell-cell fusion and pathogenicity.

(Andersen *et al*., 2020; Wall *et a*l., 2020)



ACE2 receptors are present in a wide variety of human cells revealing the potential risks of COVID-19



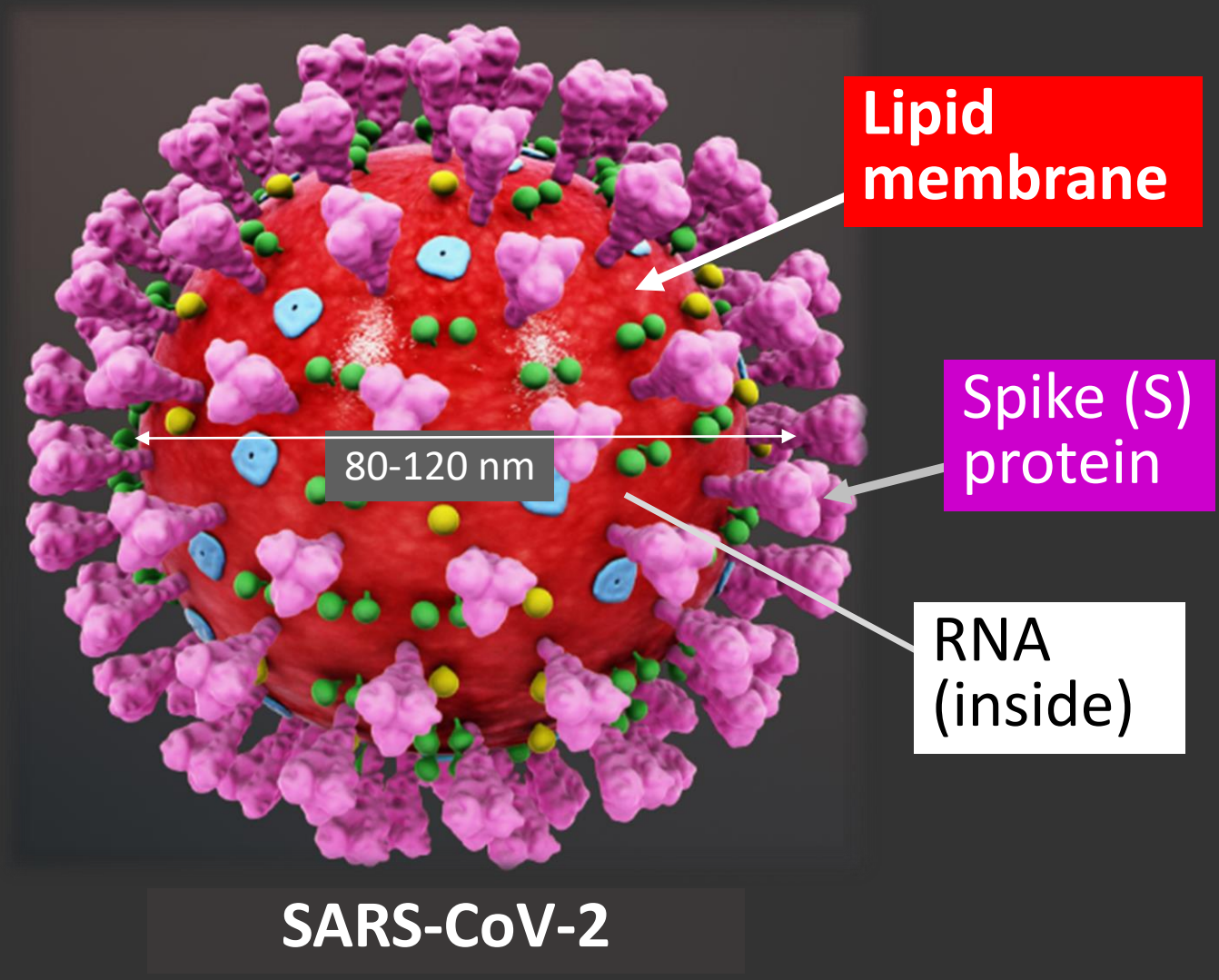


(modified from: Zou *et al.*, Front. Med. published Feb 8,2020)

Overview of Treatment Strategies

- Target proteins
- Target RNA

} Drugs Vaccines



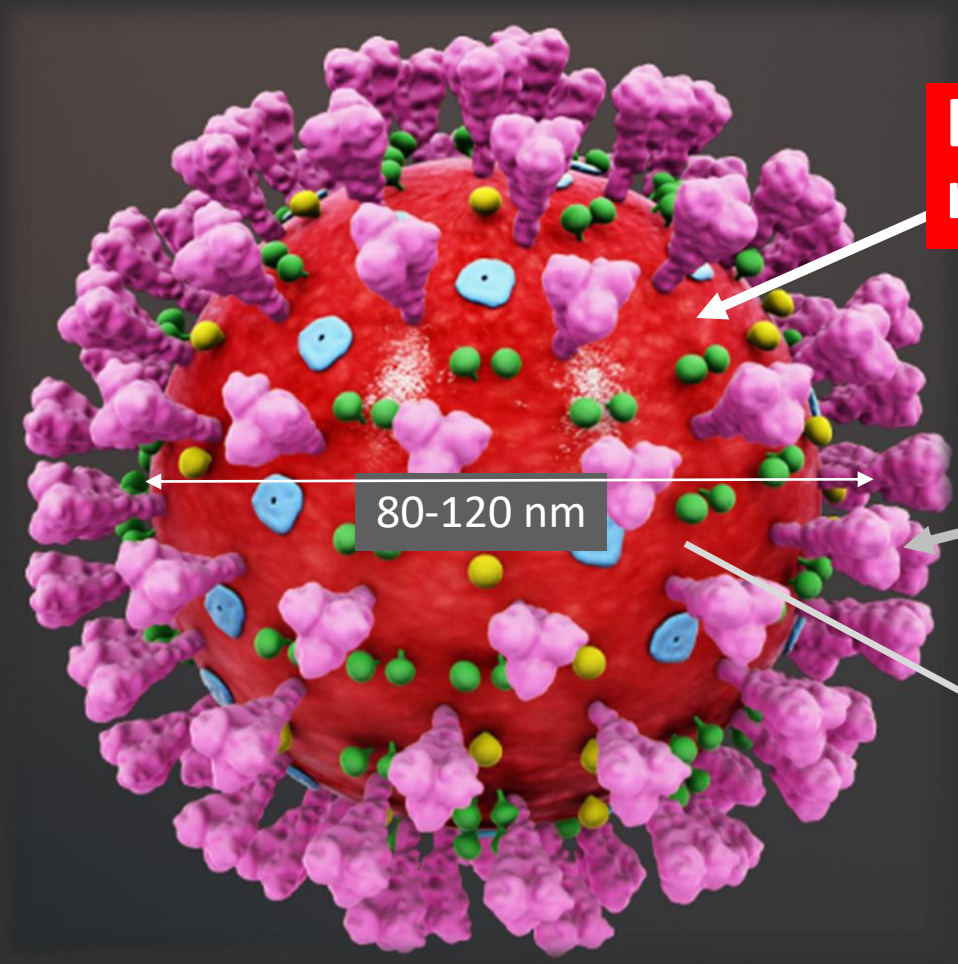
Overview of Treatment Strategies

- Target proteins
- Target RNA

} Drugs Vaccines

- Target lipid membrane ?

SARS-CoV-2 belongs to the betacoronavirus class, which can be effectively inactivated by lipid solvents (Cascella *et al.*, 2020).



SARS-CoV-2

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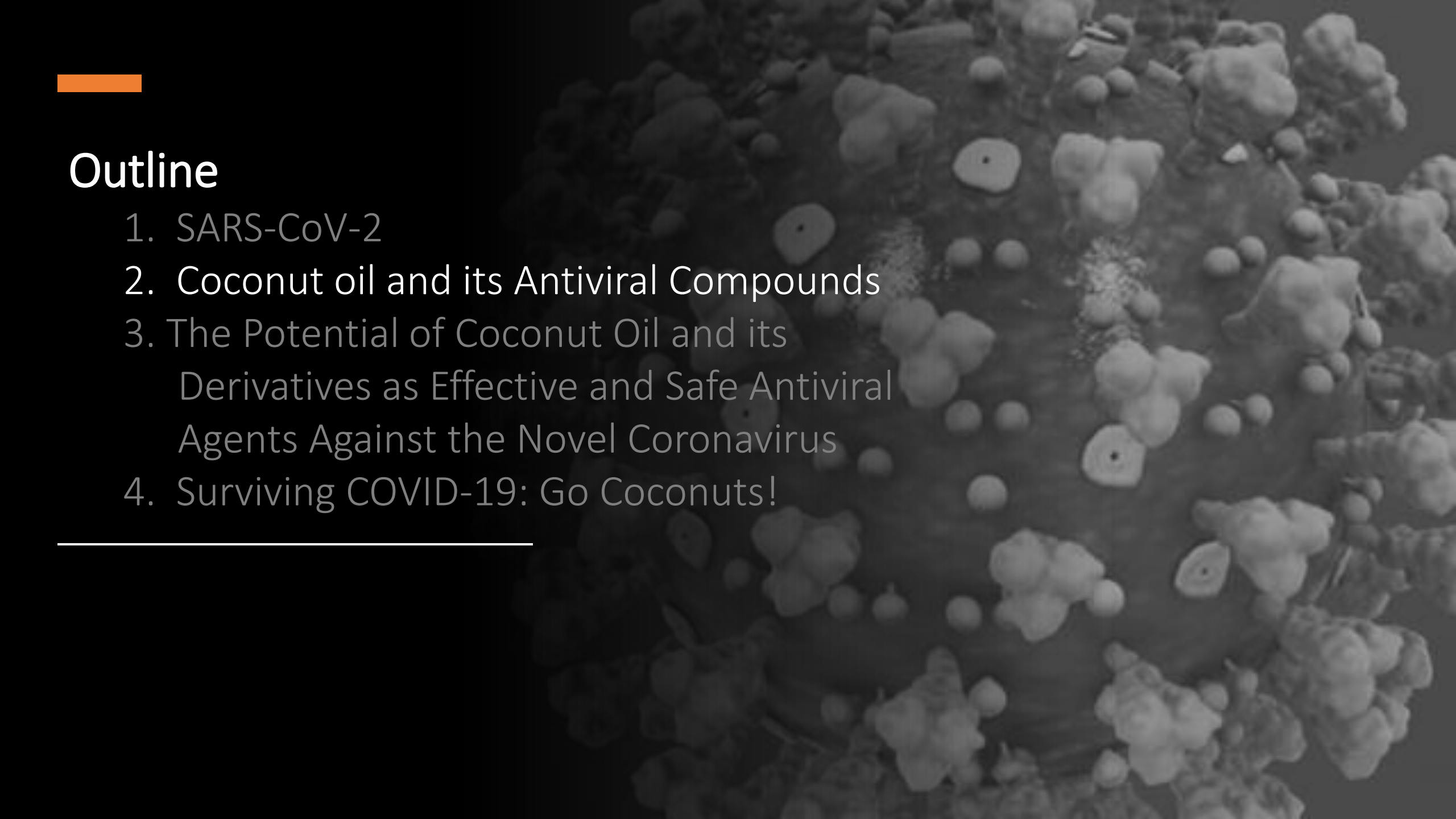

Quick facts about Coconut Oil

- The coconut has been consumed by people in the tropics for millennia. It is the basis of many of today's prominent culinary traditions. The Pacific islands would not be inhabited if there were no coconut.

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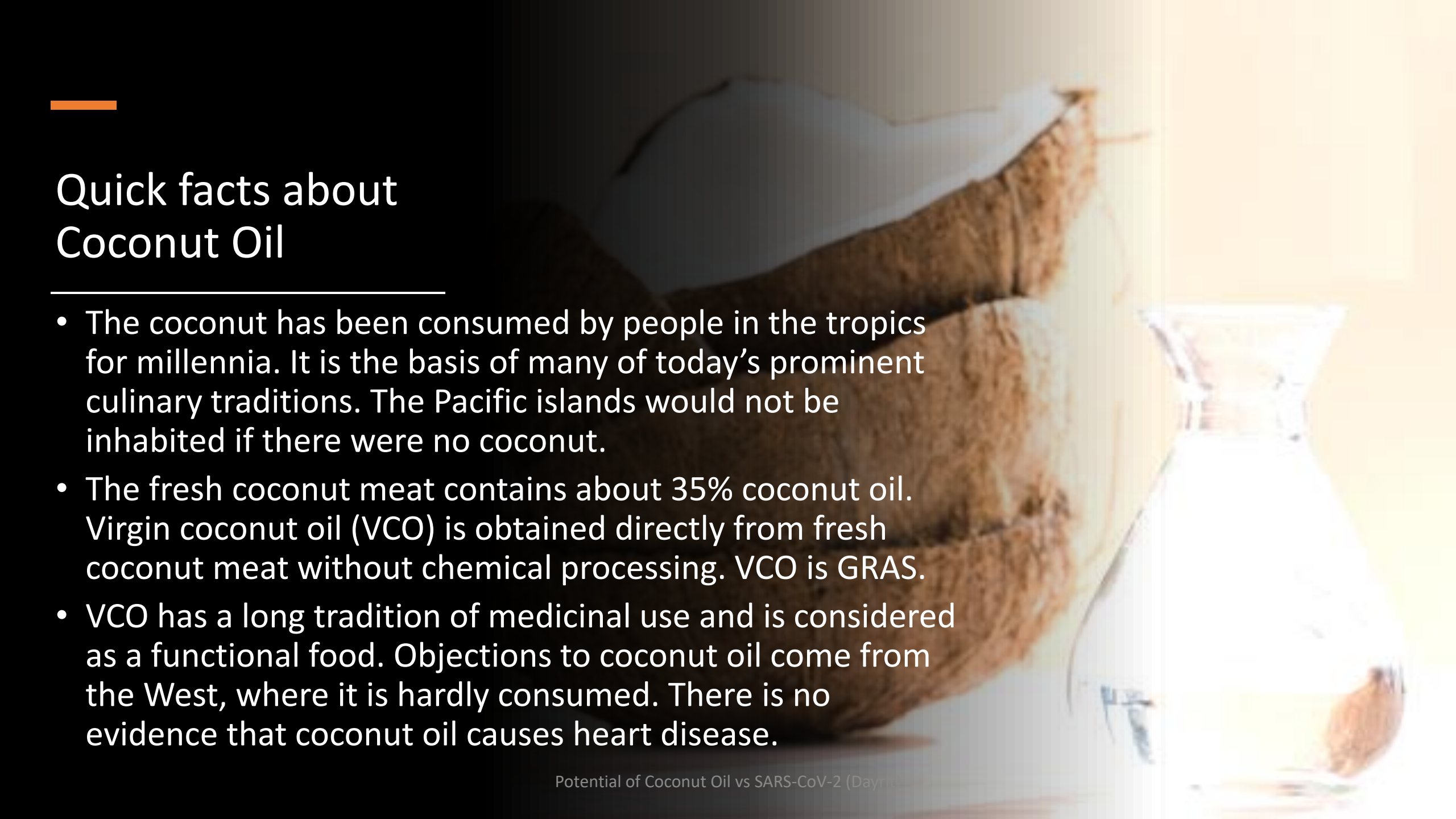
- The fresh coconut meat contains about 35% coconut oil. Virgin coconut oil (VCO) is obtained directly from fresh coconut meat without chemical processing. VCO is GRAS.
- VCO has a long tradition of medicinal use and is considered as a functional food. Objections to coconut oil come from the West, where it is hardly consumed. There is no evidence that coconut oil causes heart disease.



Coconut Oil has a unique fatty acid composition (*sui generis*)

• Caprylic	C8	7%
• Capric	C10	8%
• **Lauric**	**C12**	**48%**
• Myristic	C14	16%
• Palmitic	C16	9.5%
• Stearic	C18	3%
• Oleic	C18:1	7.5%
• Linoleic	C18:2	1.5%

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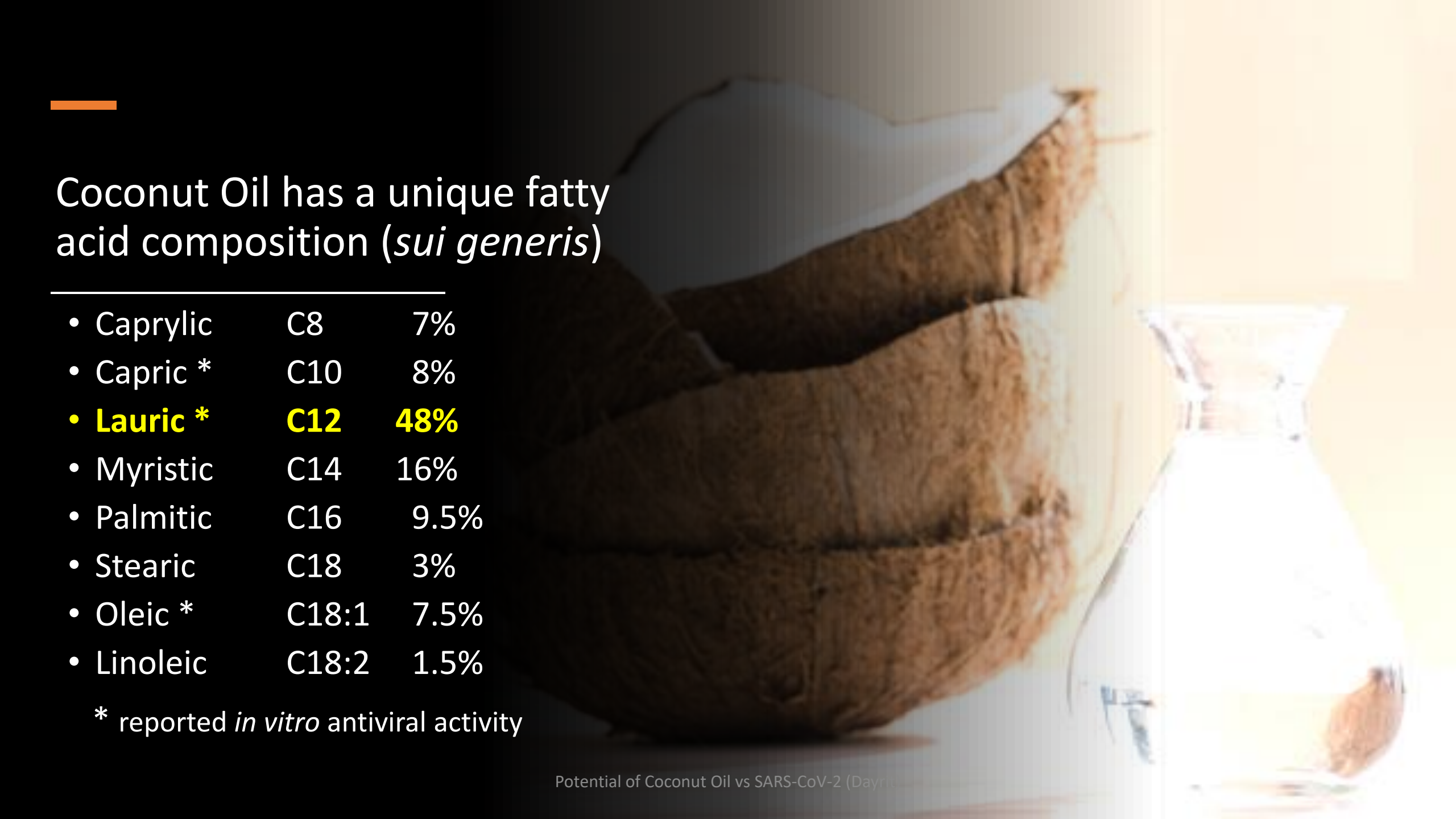
* reported *in vitro* antiviral activity



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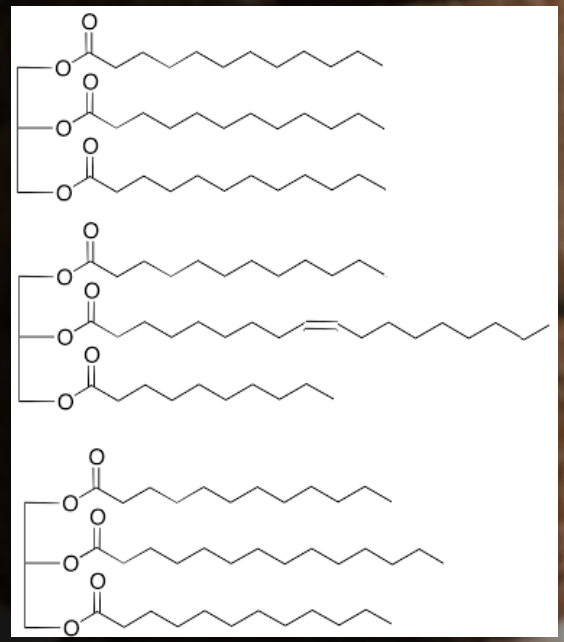
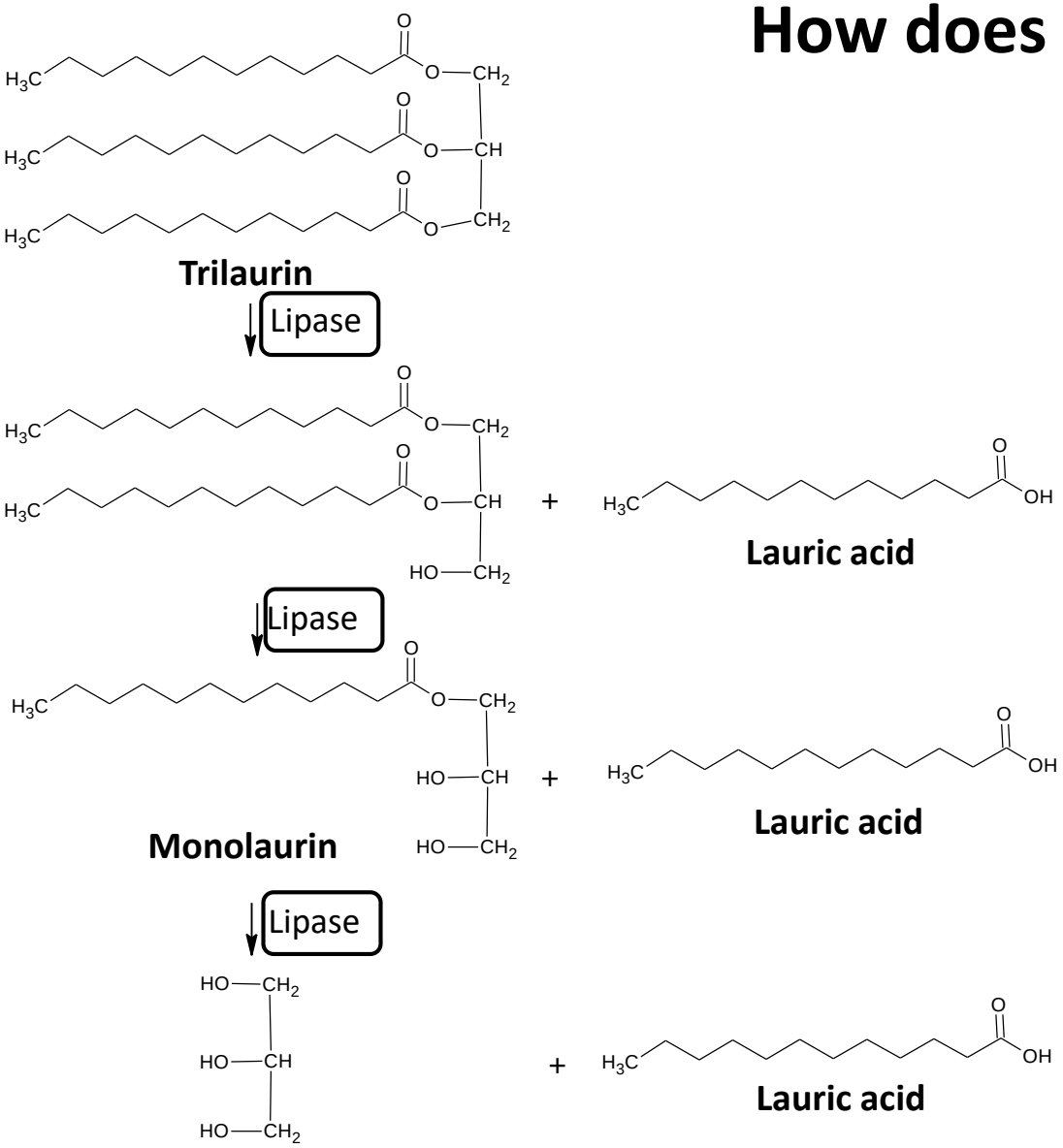
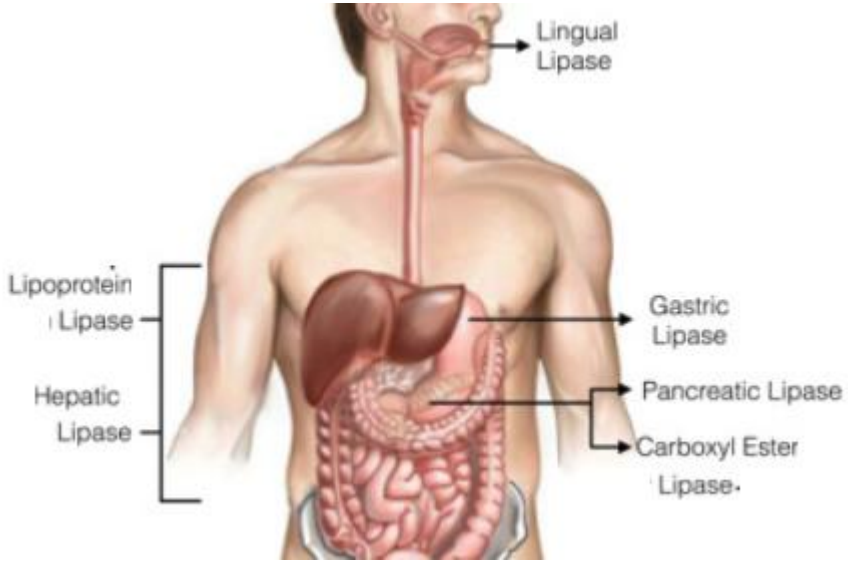
Fatty acids are present in the oil as a mixture of triglycerides



How does Coconut Oil become antiviral?



- Lipase enzyme is present in many parts of the body: saliva, skin, digestive system, liver, blood vessels



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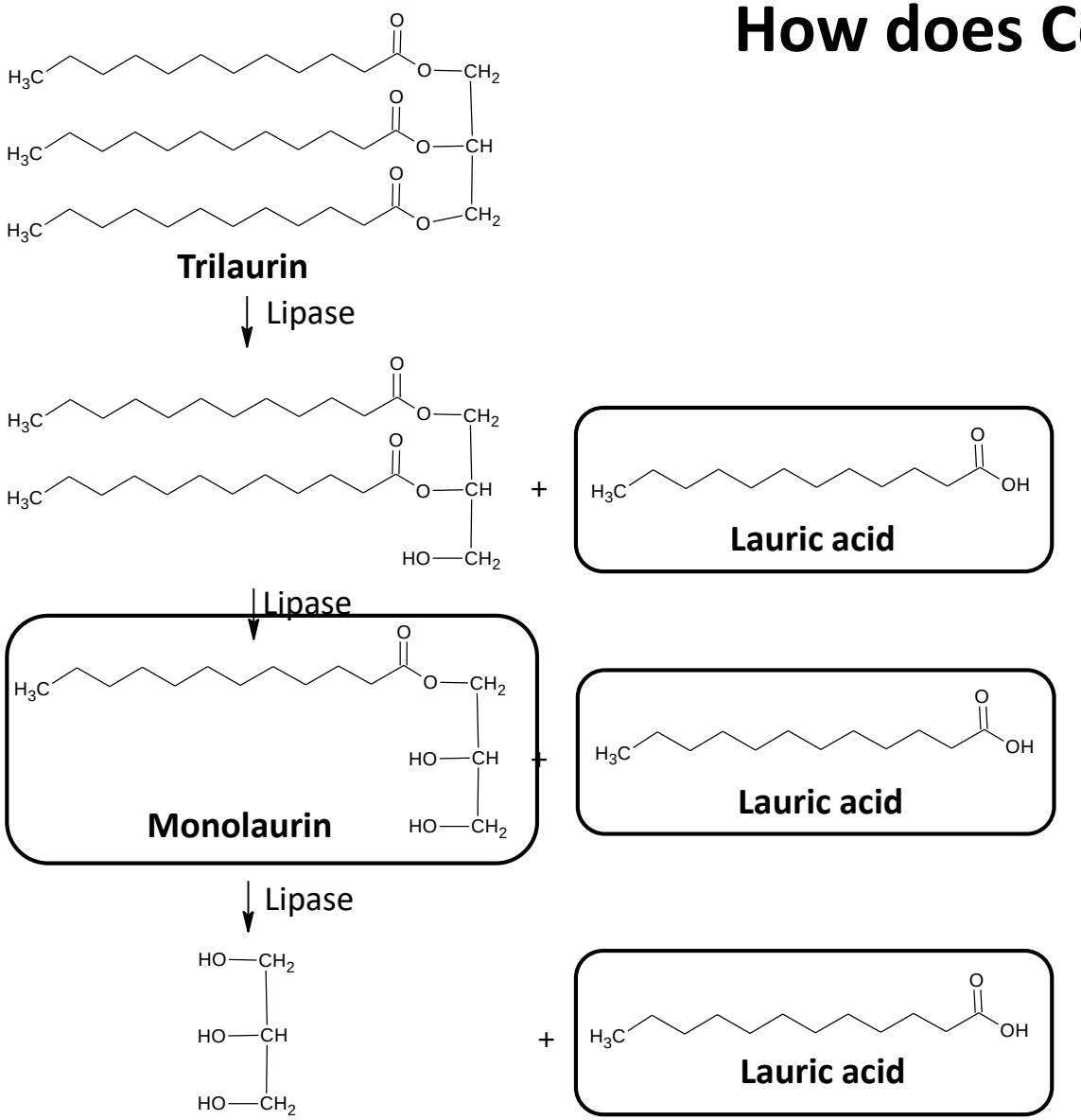
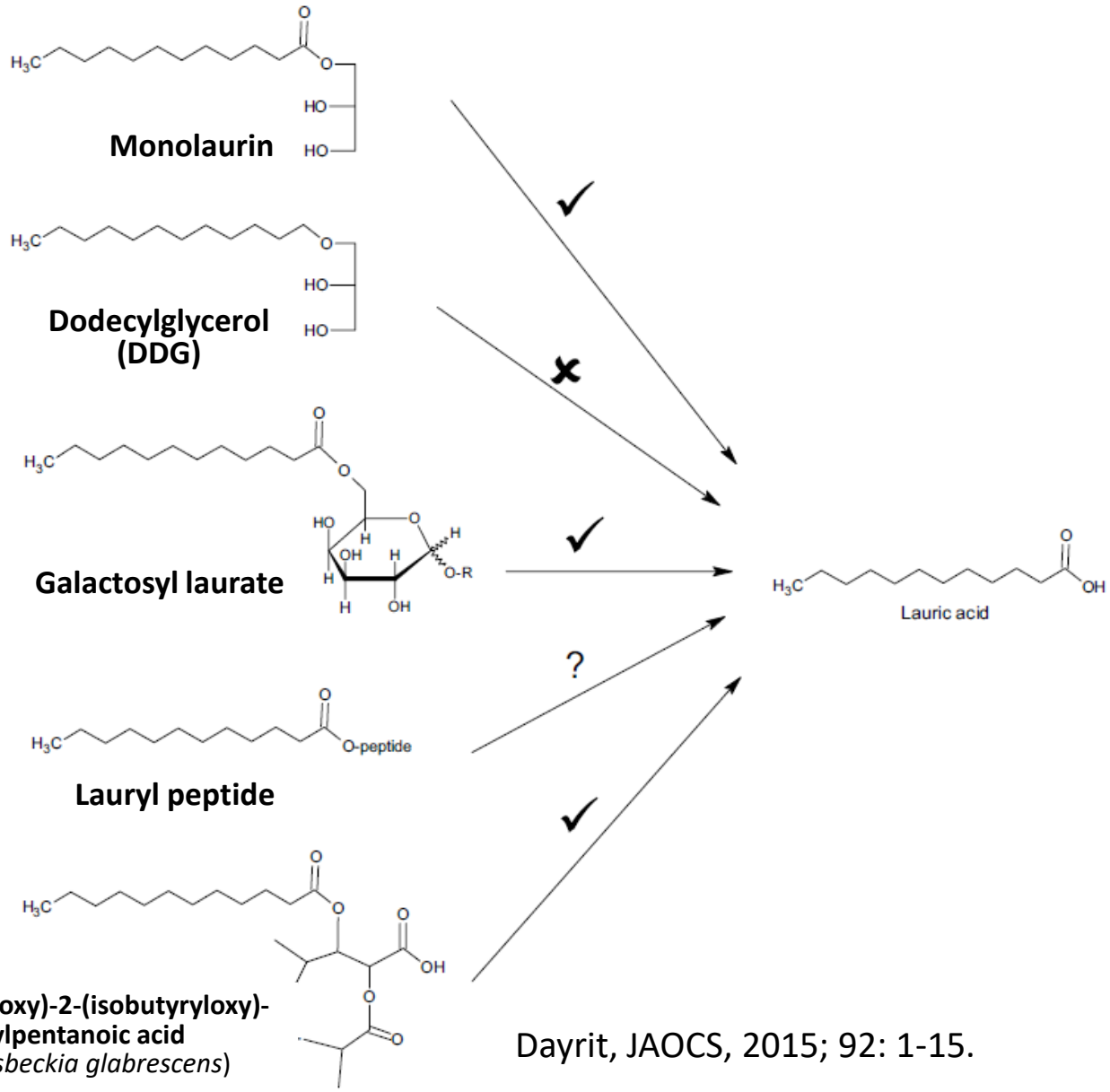


- Coconut oil becomes antibacterial and antiviral after *in vivo* hydrolysis with lipase enzyme
- The antibacterial and antiviral compounds include monolaurin, lauric acid, monocaprin, capric acid, providing wide spectrum activity.
- Coconut oil is 45-53% lauric acid (C12) and 7-8% capric acid (C10).

Antimicrobial Lauryl ester derivatives: Designed by Nature

- Natural double-action antimicrobial: Lauryl ester derivatives, which themselves are antimicrobial, undergo hydrolysis by lipase to release lauric acid, another antimicrobial compound, inside the cell.
- All of the compounds on the left column are antimicrobial. Compounds with ✓ undergo hydrolysis and release lauric acid.

✘DDG is active, but it cannot be hydrolyzed to lauric acid.



Dayrit, JAOCS, 2015; 92: 1-15.

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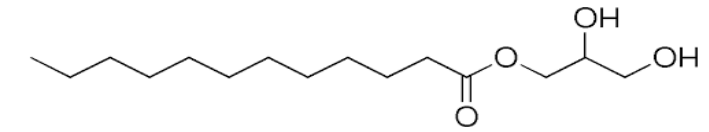
OPEN ACCESS Freely available online October 2009 | Volume 4 | Issue 10 | e7499 PLoS one

Glycerol Monolaurate and Dodecylglycerol Effects on *Staphylococcus aureus* and Toxic Shock Syndrome Toxin-1 In Vitro and In Vivo

Ying-Chi Lin[1], Patrick M. Schlievert[2], Michele J. Anderson[1], Christina L. Fair[1], Matthew M. Schaefers[1], Ramaiah Muthyala[1,3], Marnie L. Peterson[1,2]*



Monolaurin (Glycerol monolaurate)

Dodecylglycerol (DDG)

ML was compared with dodecylglycerol (DDG), a C12 monoether, for its effects on *S. aureus* growth, exotoxin production, and stability.

- *In vitro*, DDG was stable to *S. aureus* lipase and had higher inhibitory effect than ML.
- However, *in vivo* ML was more effective than DDG in reducing mortality, and suppressing TNF-α, ***S. aureus*** growth and exotoxin production. *In vivo*, ML is more effective than DDG.

Lipase hydrolysis of Coconut Oil produces a cocktail of potentially active FAs and MGs

A mixture of FAs and MAGs potentially provide broader range of activity and synergistic activity

- The mixture of monoacylglycerols (MAGs) from coconut oil was more effective than ML alone against *L. monocytogenes*. Certain combinations of the MAGs, particularly monocaprin and ML, showed synergistic activity. (Wang, 1993)

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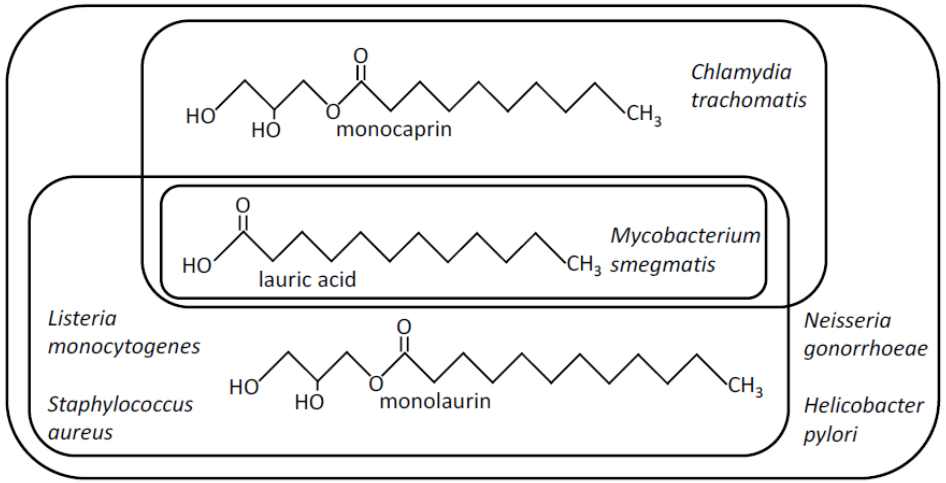
- Activity of antimicrobial fatty acid and monoglycerides, and their combination, against different bacteria. (Churchward *et al*., 2018)



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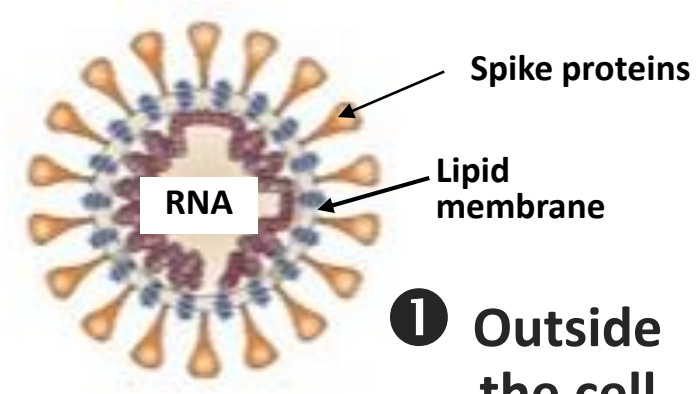
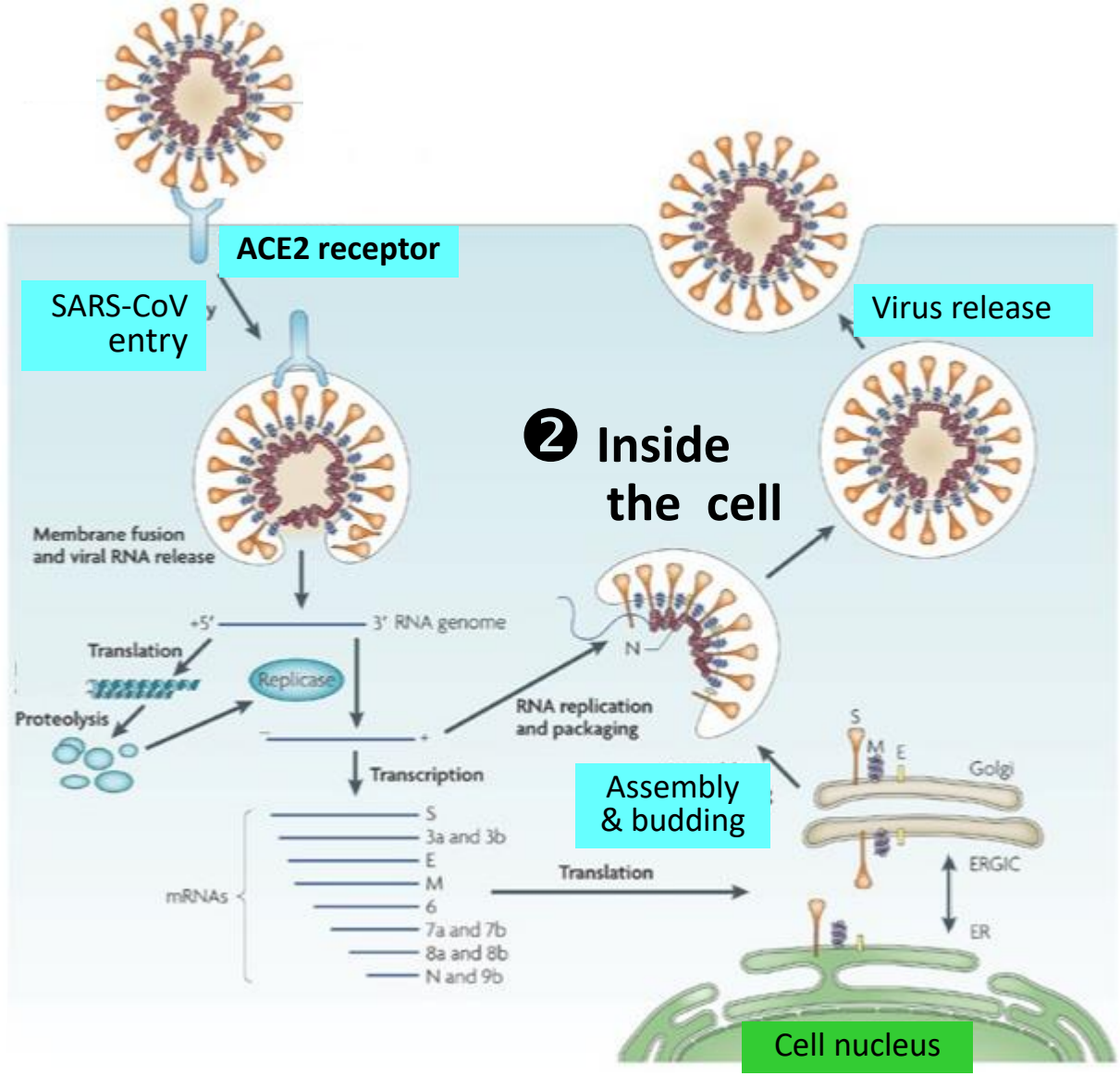


❶ Outside the cell

Possible mechanisms

❶ Disintegrates viral membrane

❷ Inhibits virus maturation



(from: Du et al., Nat Rev Microbio, 2009)

Journal of Food Safety 4 (1982) 1—12.

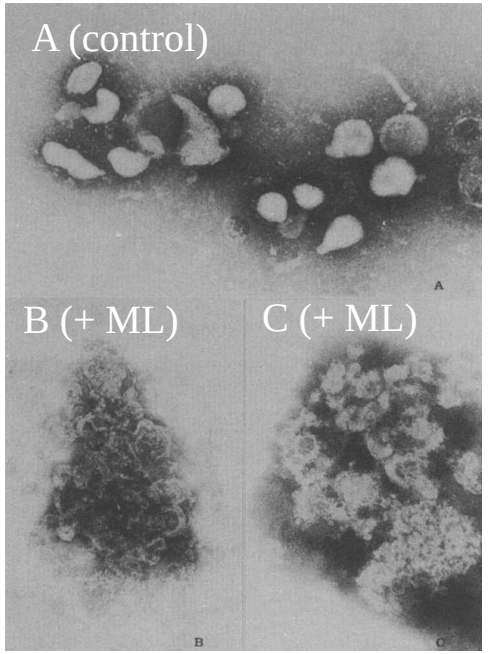
IN VITRO EFFECTS OF MONOLAURIN COMPOUNDS ON ENVELOPED RNA AND DNA VIRUSES[1]

JOHN C. HIERHOLZER
Respiratory Virology Branch
Center for Disease Control
Atlanta, Georgia 30333

JON J. KABARA
Department of Biomechanics
Michigan State University
East Lansing, Michigan 48824

Possible mechanisms

❶ Disintegrates viral membrane



Monolaurin reduced infectivity of 14 human RNA and DNA enveloped viruses in cell culture by >99.9%. Monolaurin acted by disintegrating the virus envelope (Hierholzer & Kabara, 1982).

Activity against coronavirus 2293 (magnification: x 140,000)
(A) Treated with ethanol (control)
(B) Treated with monolaurin solution 1
(C) Treated with monolaurin solution 2

(Hierholzer & Kabara, 1982)

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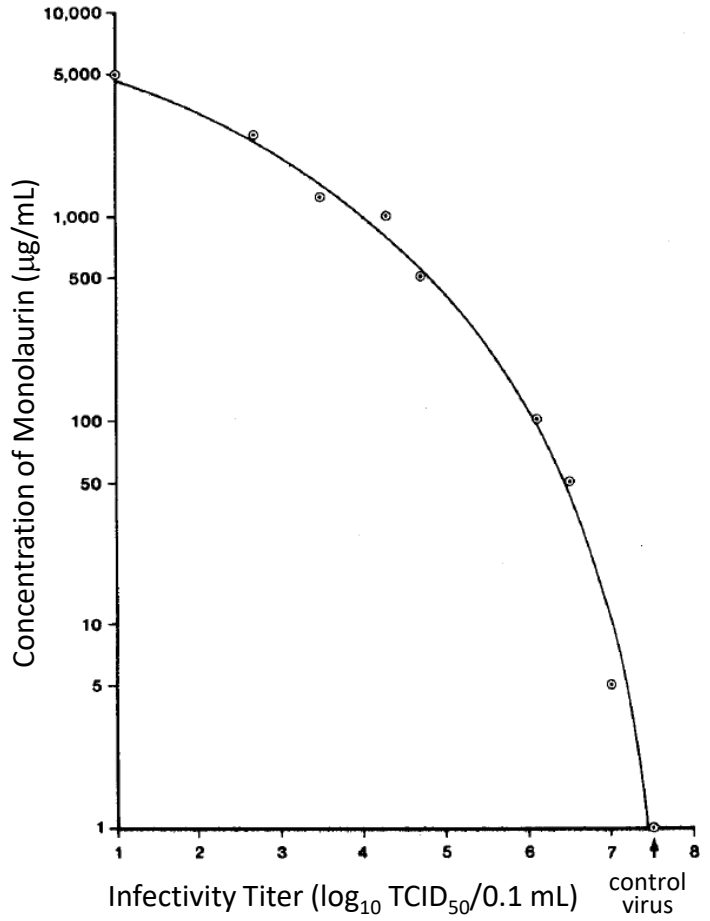


In vitro infectivity of Herpes simplex Type 1 virus against varying concentrations of monolaurin in human lung (HELF) cells. (Hierholzer & Kabara, 1982)

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Jan. 1987, p. 27–31 Vol. 31, No. 1

Inactivation of Enveloped Viruses and Killing of Cells by Fatty Acids and Monoglycerides

HALLDOR THORMAR,[1,2]* CHARLES E. ISAACS,[1] HANNAH R. BROWN,[1] MARC R. BARSHATZKY,[1] AND TAMMY PESSOLANO[1]

Possible mechanisms

❶ Disintegrates viral membrane

TABLE 2. Viral inactivation by incubation with fatty acids at 37°C for 30 min

Fatty acid	Concn[a] in mg/ml (mM)	Reduction of virus titer (log_{10})		
		VSV	HSV-1	VV[b]
Caprylic (8:0)	10 (69)	1.8	ND	≥3.2
Capric (10:0)	4 (22)	≥4.0[c]	≥4.0	≥3.2
Lauric (12:0)	2 (10)	≥4.0	≥4.0	≥3.2
Myristic (14:0)	4 (16)	≥4.0	≥4.0	1.7
Palmitic (16:0)	20 (78)	1.0	1.0	0.7
Stearic (18:0)	20 (70)	0	ND	ND

VSV: vesicular somatitis virus; HSV-1: herpes simplex virus type 1; VV: visna virus

- Medium-chain saturated and long-chain unsaturated fatty acids were all highly active against the enveloped viruses.
- Monoglycerides of these fatty acids were also highly antiviral.
- Antiviral fatty acids caused leakage of the viral envelope at lower concentrations, and complete disintegration of the envelope and the viral particles at higher concentrations.

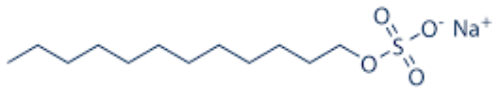
Possible mechanisms

❶ Disintegrates viral membrane

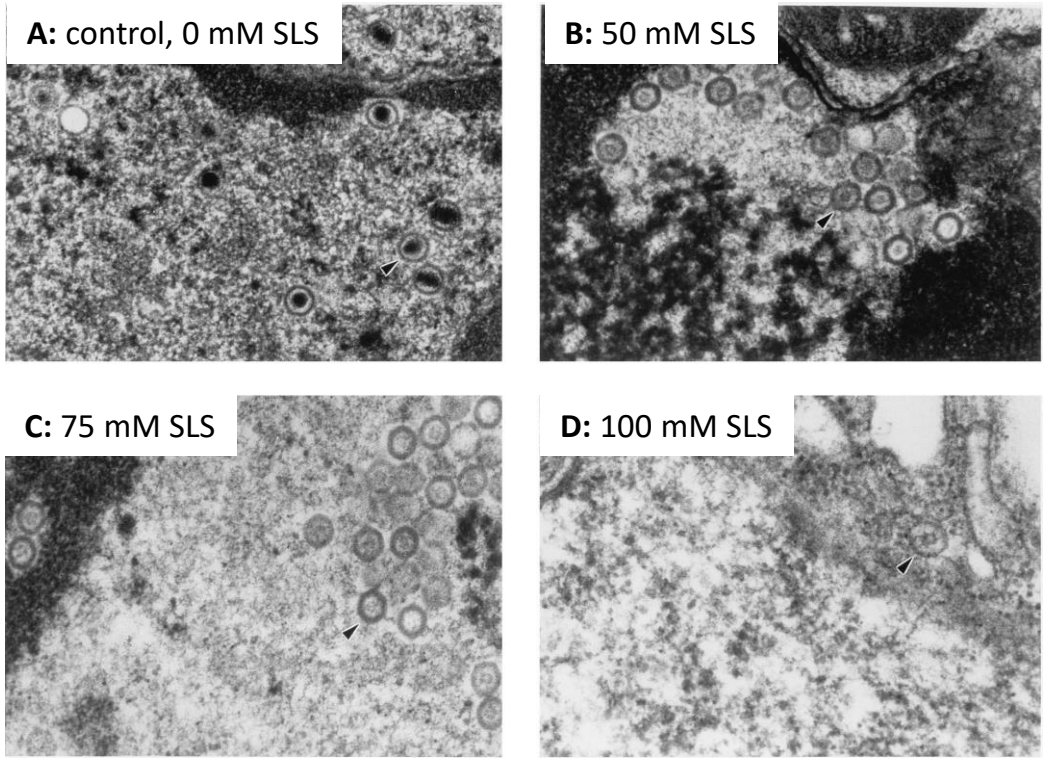
JOURNAL OF CLINICAL MICROBIOLOGY, Jan. 2000, p. 110–119 Vol. 38, No. 1

In Vitro and In Vivo Evaluations of Sodium Lauryl Sulfate and Dextran Sulfate as Microbicides against Herpes Simplex and Human Immunodeficiency Viruses

JOCELYNE PIRET,[1] JULIE LAMONTAGNE,[1] JULIE BESTMAN-SMITH,[1] SYLVIE ROY,[1] PIERRETTE GOURDE,[1] ANDRÉ DÉSORMEAUX,[1] RABEEA F. OMAR,[1] JULIANNA JUHÁSZ,[2] AND MICHEL G. BERGERON[1]*



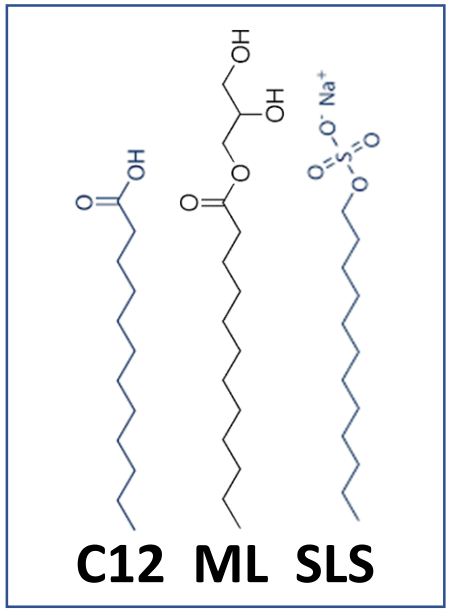
Sodium lauryl sulfate



Electron micrographs of Vero cells infected with HSV-1, pretreated for 1 h at 37°C with SLS: 0 mM (**A**, control), 50 mM (**B**), 75 mM (**C**), and 100 (D) mM. (Magnification: x52,500. (Piret, 200)

Sodium lauryl sulfate (SLS) solubilized and denatured the viral envelope *inside* the infected cell (Piret 2000, 2002).

Surfactant 101



Surfactant

Polar head group

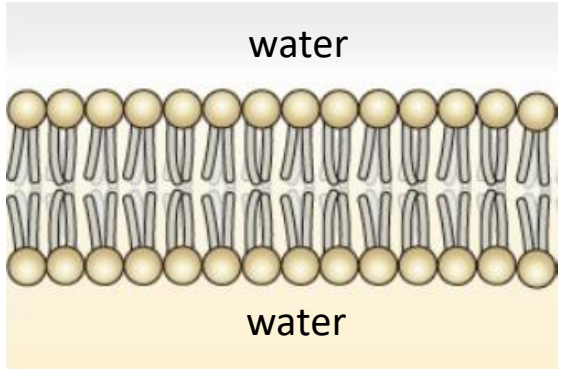
Nonpolar tail

Phospholipid (component of cell membrane)

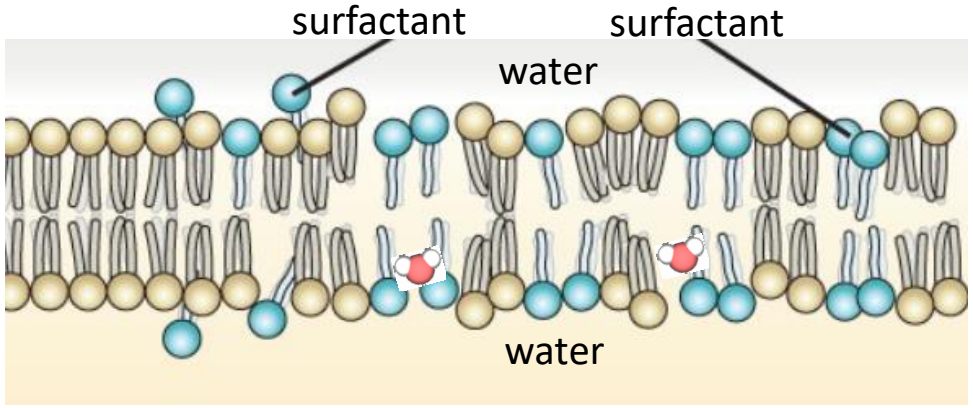
Polar head group

Nonpolar double tail

Lipid bilayer (virus membrane)

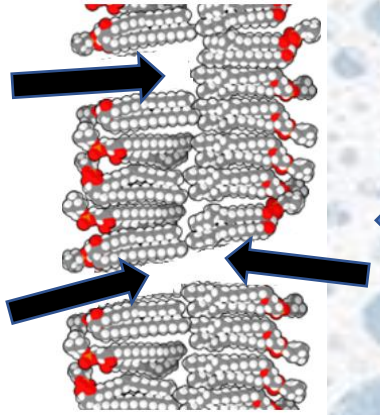


Surfactants disrupt the lipid bilayer

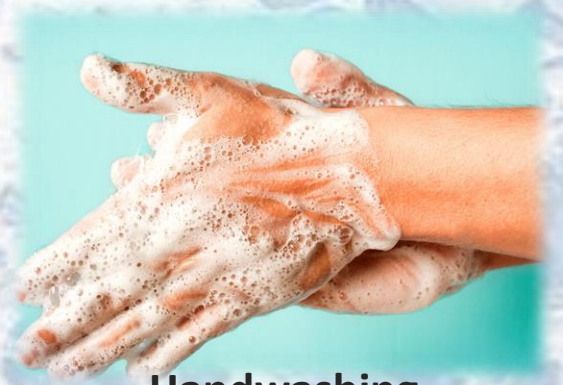


Possible mechanisms

❶ Disintegrates viral membrane



Damaged lipid bilayer



Handwashing

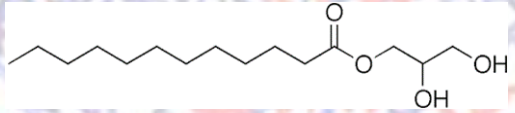
Soap kills the virus by destroying the lipid membrane

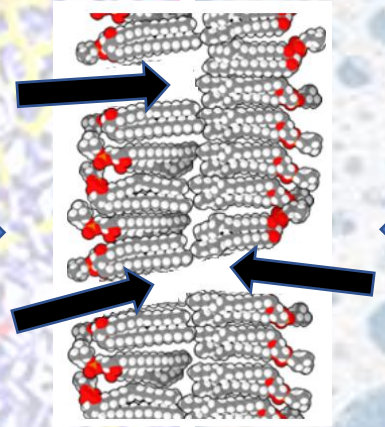
Possible mechanisms

❶ Disintegrates viral membrane

Coconut oil

Lipase





Damaged lipid bilayer

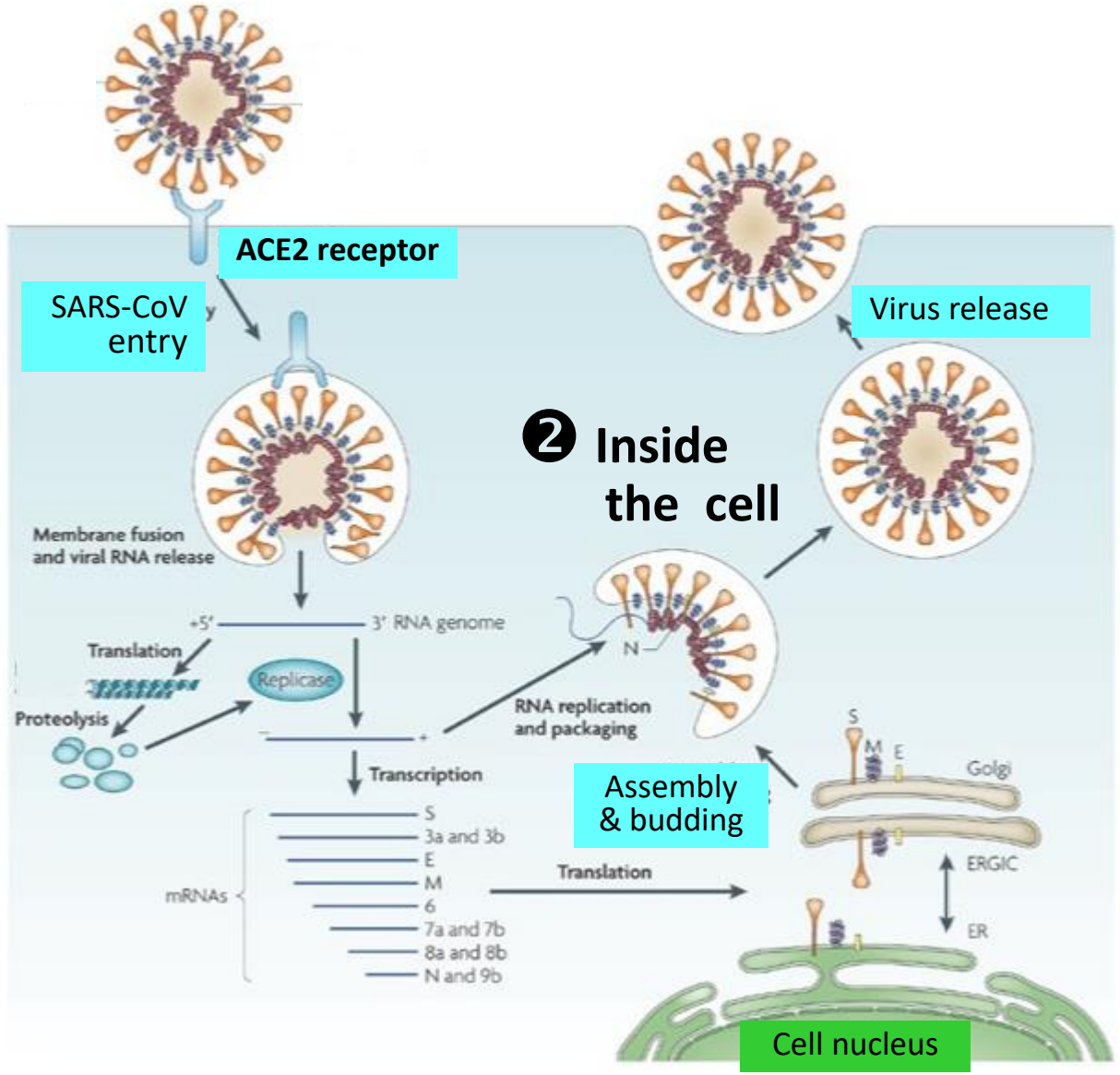
Handwashing

Compounds from coconut oil (e.g., monolaurin) kill the virus by destroying the lipid membrane

Soap kills the virus by destroying the lipid membrane

Possible mechanisms

❷ Inhibits virus maturation



(from: Du et al., Nat Rev Microbio, 2009)

Possible mechanisms

❷ Inhibits virus maturation

Journal of General Virology (1994), **75**, 353–361.

Lauric acid inhibits the maturation of vesicular stomatitis virus

Beate Hornung, Eberhard Amtmann and Gerhard Sauer*

- In the presence of C12, the production of infectious VSV was inhibited in a dose-dependent manner. Those with shorter or longer chains were less effective or had no antiviral activity.
- Analysis of the antiviral mechanism of C12 revealed that the correct assembly of the viral components was disturbed.
- C12 prevented the binding of M protein to the host cell membrane, where the protein plays an essential role in virus assembly. Thus, treatment of VSV-infected cells with C12 resulted in inhibition of virus release.

Possible mechanisms

❷ Inhibits virus maturation

Journal of General Virology (1994), **75**, 353–361.

Lauric acid inhibits the maturation of vesicular stomatitis virus

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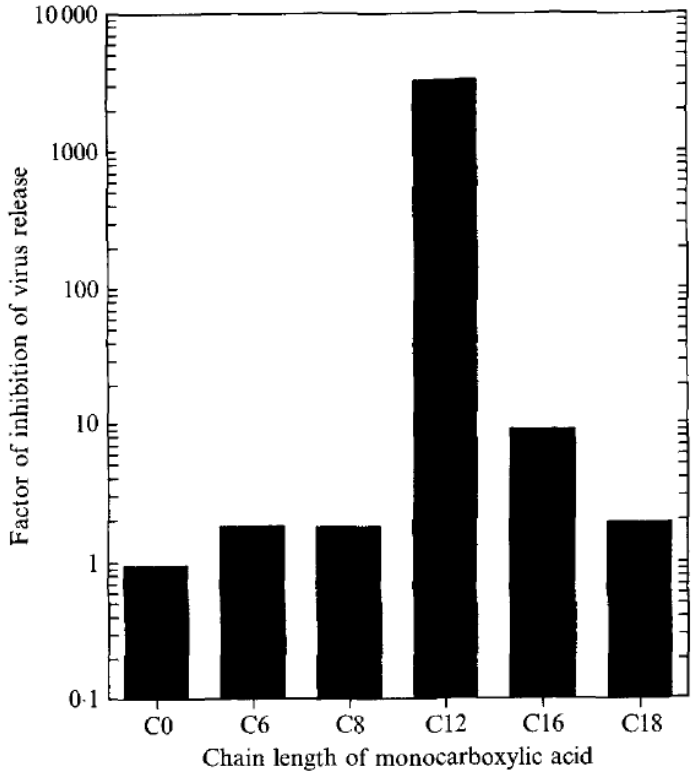
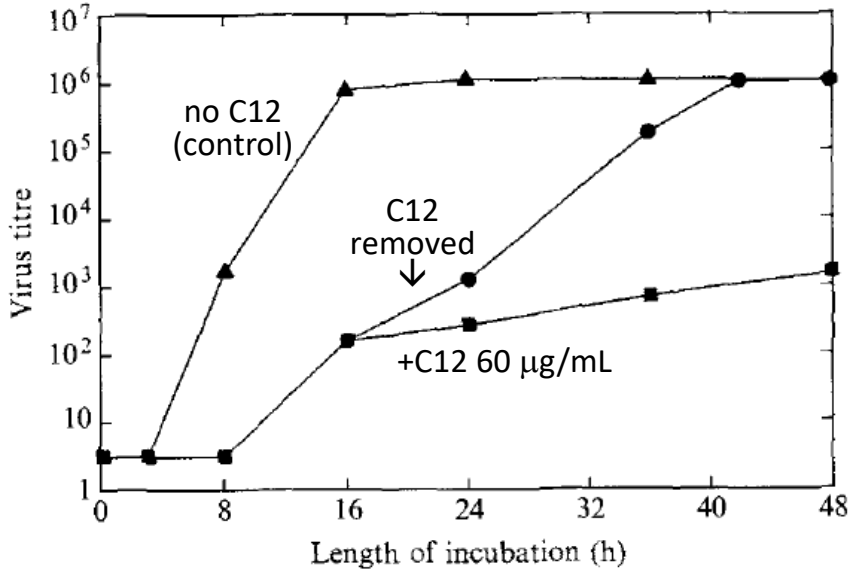


Influence of chain length on replication of VSV, incubated with 60 μg/mL of each fatty acid.
(Note: y-axis is logarithmic.)



C12 inhibits VSV replication. Rita cells were infected with VSV and incubated in the absence (▲) or presence (■) of 60 μg/mL C12. (●) After 16 h of C12 treatment, a portion was withdrawn and grown with C12-free medium.

Possible mechanisms

❷ Inhibits virus maturation

Arch Virol (2001) 146: 777–790

Effect of fatty acids on arenavirus replication: inhibition of virus production by lauric acid

S. Bartolotta, C. C. García, N. A. Candurra, and E. B. Damonte

- Saturated fatty acids (C10–C18) were evaluated for their inhibitory activity against the multiplication of Junin virus (JUNV). The most active inhibitor was C12, which reduced virus yields of pathogenic strains of JUNV in a dose-dependent manner, without affecting cell viability. Fatty acids with shorter or longer chain length had a reduced or negligible anti-JUNV activity.
- From mechanistic studies, it was concluded that C12 inhibited a late maturation stage in the replicative cycle of JUNV. Viral protein synthesis was not affected by the compound, but the expression of glycoproteins in the plasma membrane was diminished.
- C12-induced effects were dependent on the continued presence of the fatty acid.

Possible mechanisms

❷ Inhibits virus maturation

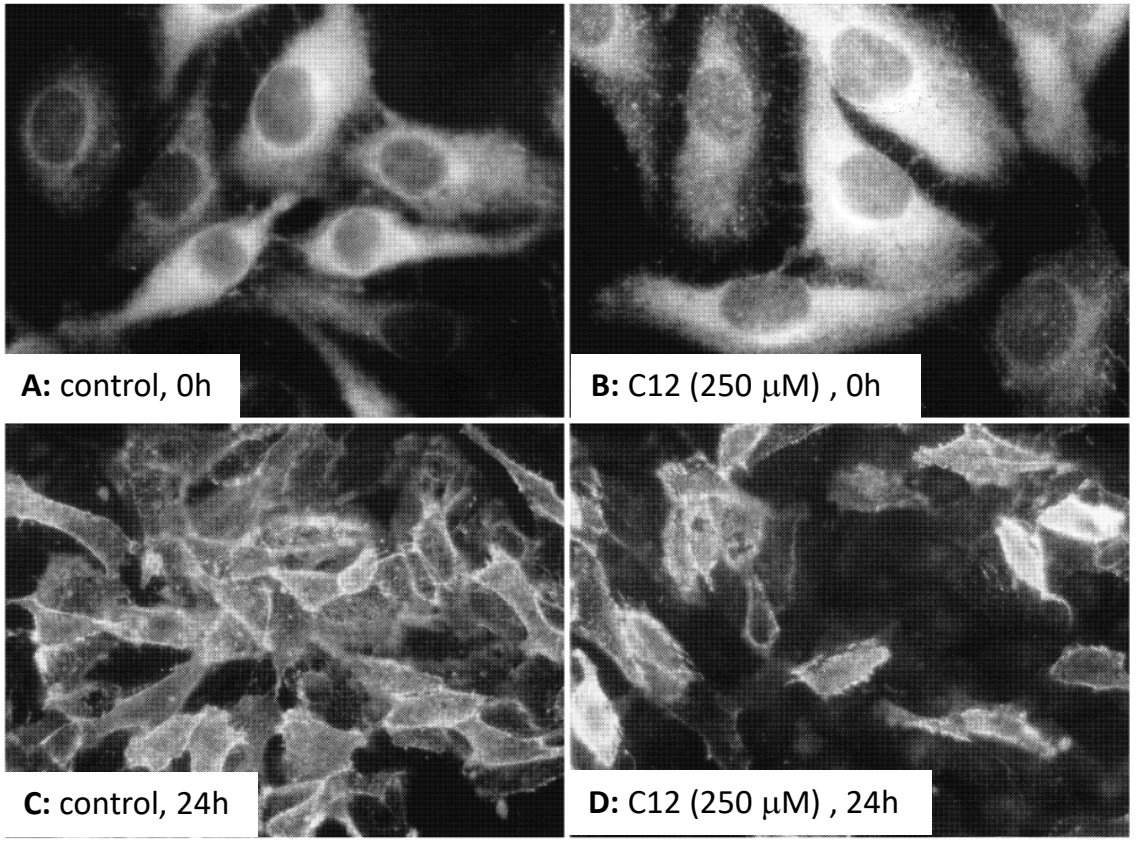
Vero cells were infected with JUNV over 24h:
in the absence (**A**, **C**)
or presence of C12 (250 μM) (**B**, **D**).

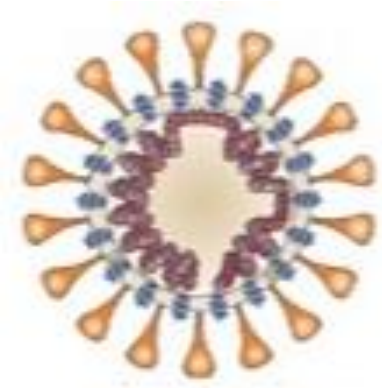
C12 interfered with the expression and distribution of JUNV proteins, inhibiting viral replication.

Arch Virol (2001) 146: 777–790

Effect of fatty acids on arenavirus replication: inhibition of virus production by lauric acid

S. Bartolotta, C. C. García, N. A. Candurra, and **E. B. Damonte**



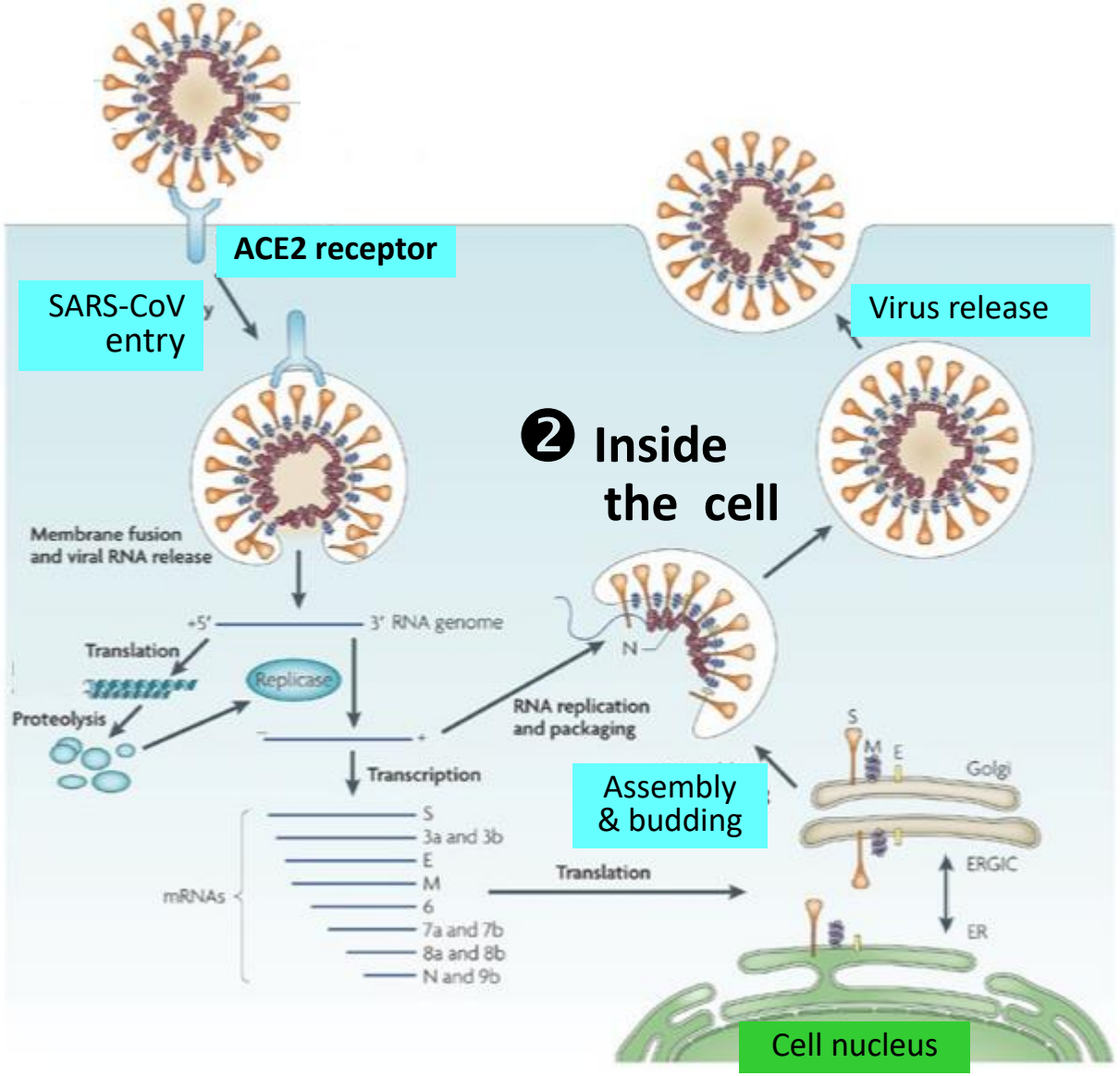


❶ Outside the cell

Possible mechanisms

❶ **Disintegrates viral membrane**
C12 and ML, which are formed upon ingestion of coconut oil, and SLS, a synthetic C12 surfactant, kill viruses by disintegration of the viral membrane.

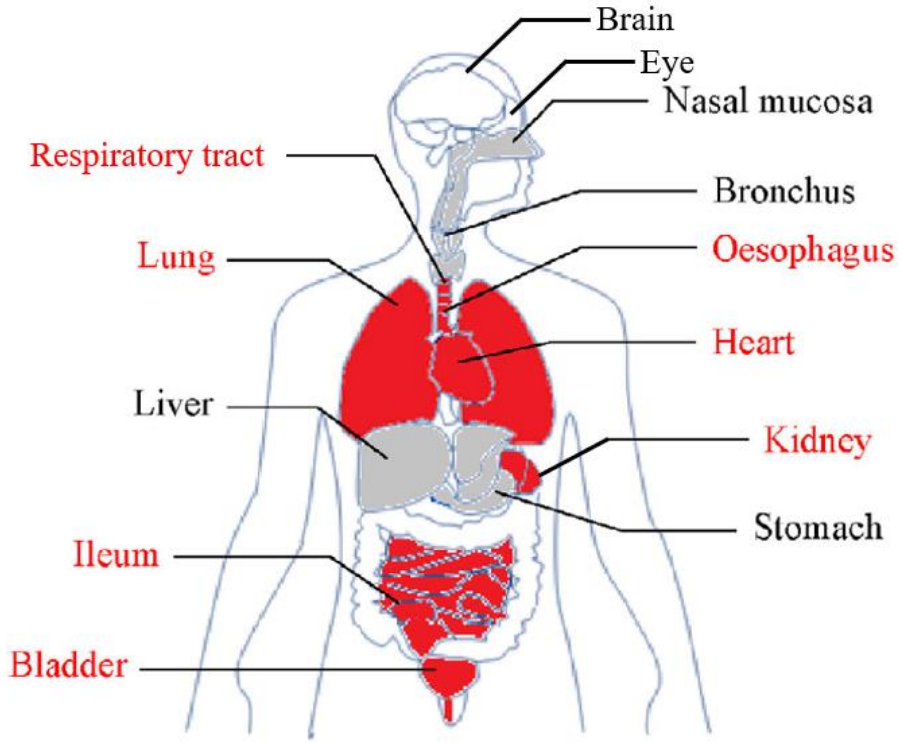
❷ **Inhibits virus maturation**
C12 can inhibit virus maturation in a dose-dependent and reversible manner.



(from: Du et al., Nat Rev Microbio, 2009)

VCO can be taken safely in a number of ways to target the organs where the ACE2 receptors are present

- Oral
- Gargling
- Oil pulling
- Nasal spray
- Eye drops



(modified from: Zou *et al*., *Front. Med*. published Feb 8,2020)

The Potential of Coconut Oil and its Derivatives as Effective and Safe Antiviral Agents Against the Novel Coronavirus (2019-nCoV)

Given the considerable scientific evidence for the antiviral activity of coconut oil, lauric acid and its derivatives and their general safety, and the absence of a cure for 2019-nCoV, we urge that clinical studies be conducted among patients who have been infected with 2019-nCoV. This treatment is affordable and virtually risk-free, and the potential benefits are enormous.

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Coconut oil is antiviral.

However, we have to determine its efficacy against COVID-19 as therapy and prophylaxis, in particular, the dosage and most effective modes of intake.

In vitro Study on the Efficacy of Lauric Acid and Derivatives Against COVID-19

(Proponent: ADMU, funded by DOST-PCHRD)

Status: On-going

DOST - PCHRD

DukeNUS Medical School

Dr. Ian Ken Dimzon

Dr. Crisanto M. Lopez
Ralph Geronimo

Dr. Erwin P. Enriquez
Candell Grace Quiño

Acknowledgements:

- Dr. Sonia Jacinto (Institute of Biology, University of the Philippines Diliman) for the Vero cells
- Ms. Lolit Lagurin, for running the NMR analyses

The Beneficial effects of VCO among Suspected and Probable Cases of COVID-19

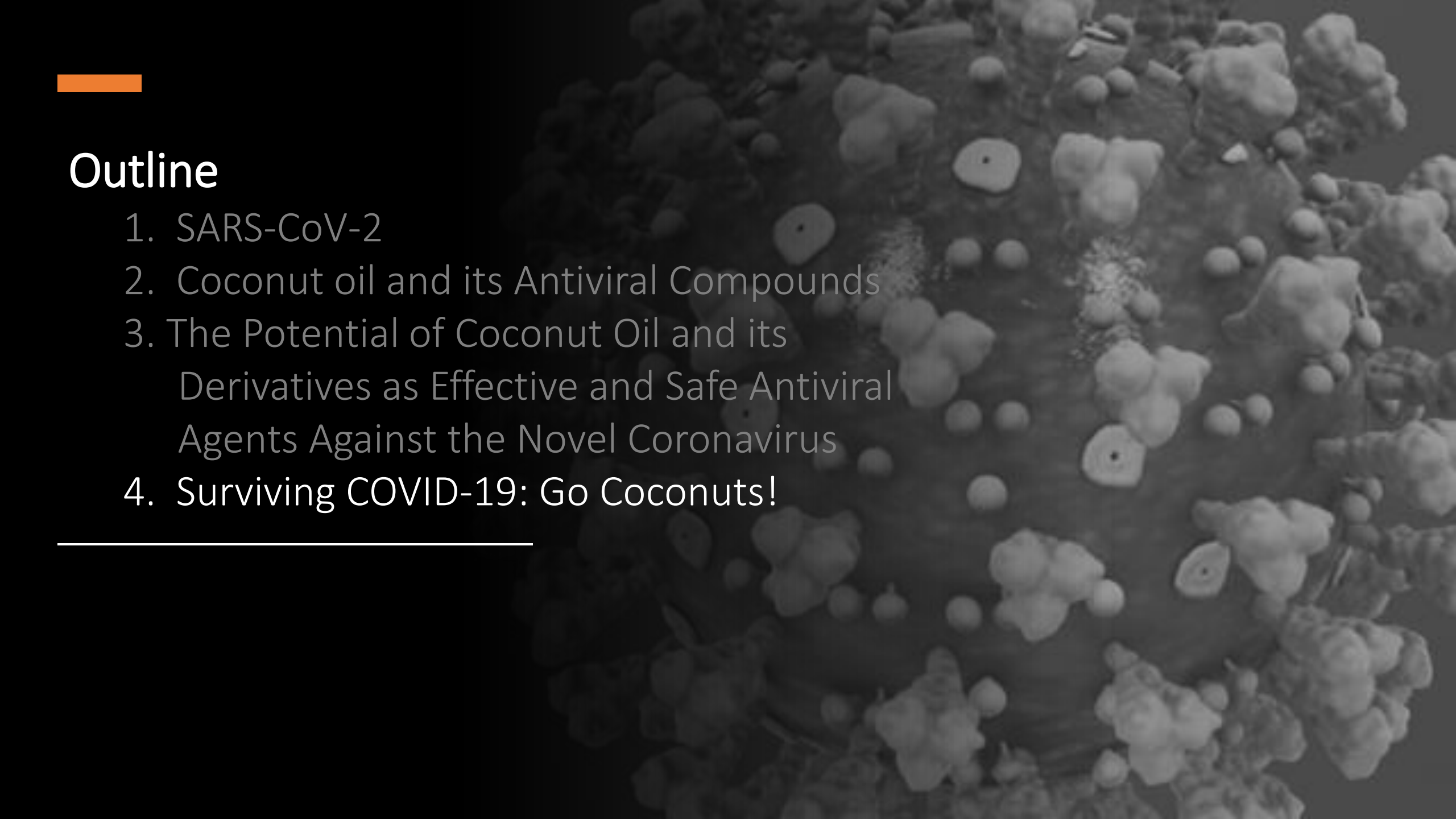
(Proponent: FNRI, funded by DOST-PCHRD, in cooperation with PCA)

Status: On-going

Virgin Coconut Oil as Adjunctive Therapy for COVID-19 Patients

(Proponent: UP-PGH, funded by DOST-PCHRD, in cooperation with PCA)

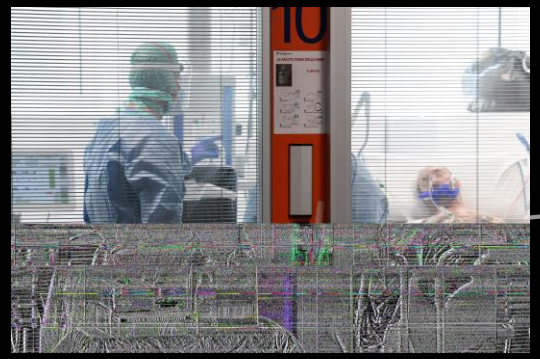
Status: Pending



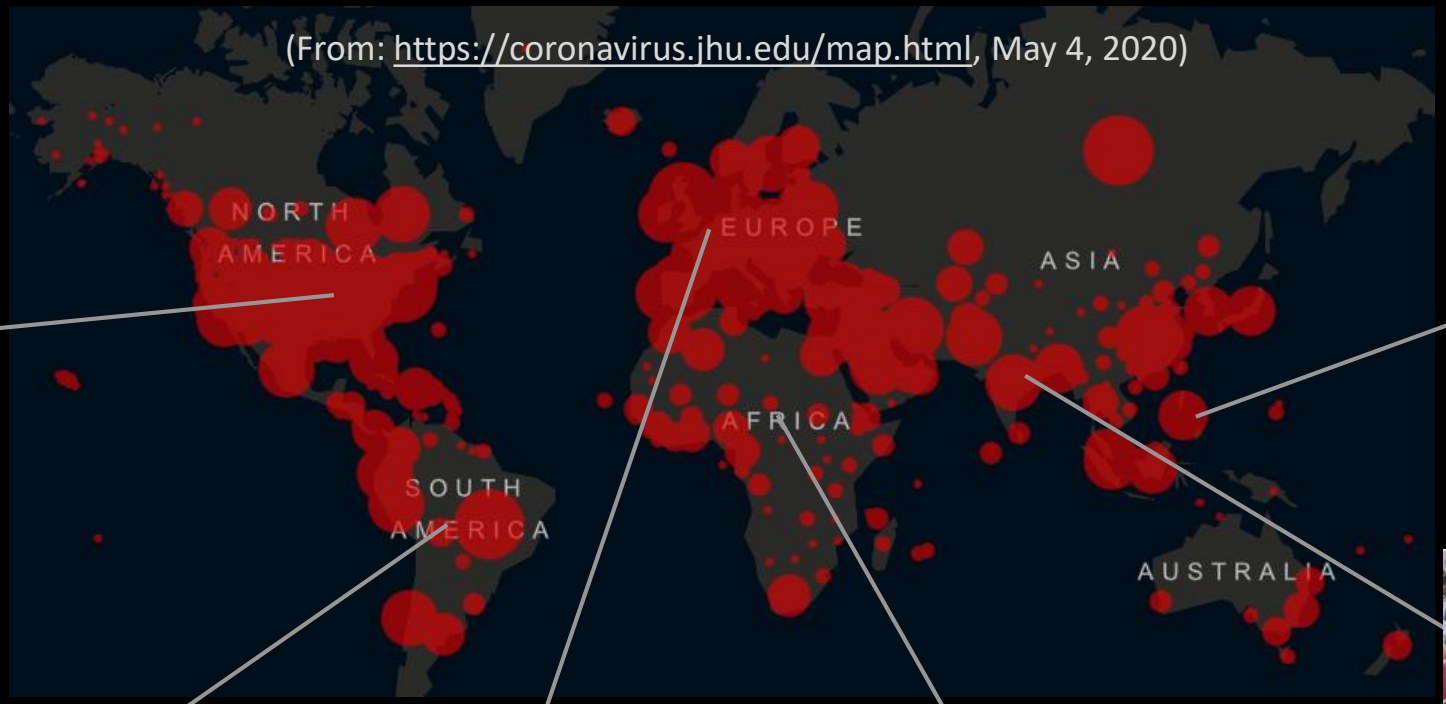
Outline

1. SARS-CoV-2
2. Coconut oil and its Antiviral Compounds
3. The Potential of Coconut Oil and its Derivatives as Effective and Safe Antiviral Agents Against the Novel Coronavirus
4. Surviving COVID-19: Go Coconuts!

Surviving COVID-19:
Solutions should be effective, affordable and appropriate



(New York City, Time Magazine)



(From: https://coronavirus.jhu.edu/map.html, May 4, 2020)

(Philippines, OneNews.PH)

(India, The Hindu)

(Rio de Janeiro City, Guardian)

(Italy, Harvard Bus. Rev.)

(Zimbabwe, AP News)

Surviving COVID-19:
Repurposing drugs and vaccines

?

Repurposing drugs

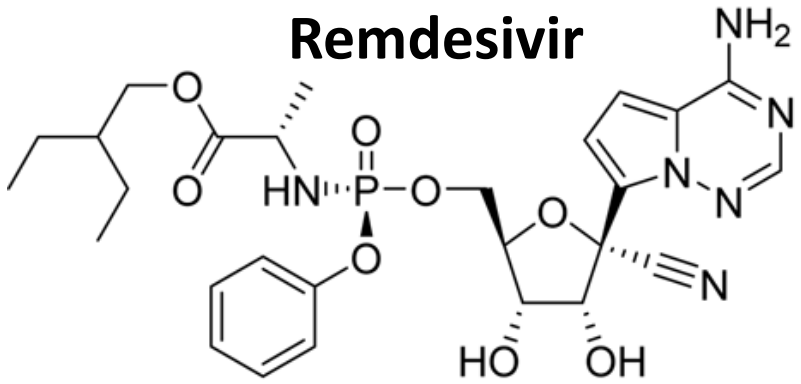
- Chloroquine
- Hydroxychloroquine
- Remdesivir®
- Sildenafil (Viagra®)
- Favipiravir (antiviral for influenza)
- Lopinavir + Ritonavir (anti-HIV)
- Ravulizumab
- Sarilumab
- … and many more

Repurposing vaccines

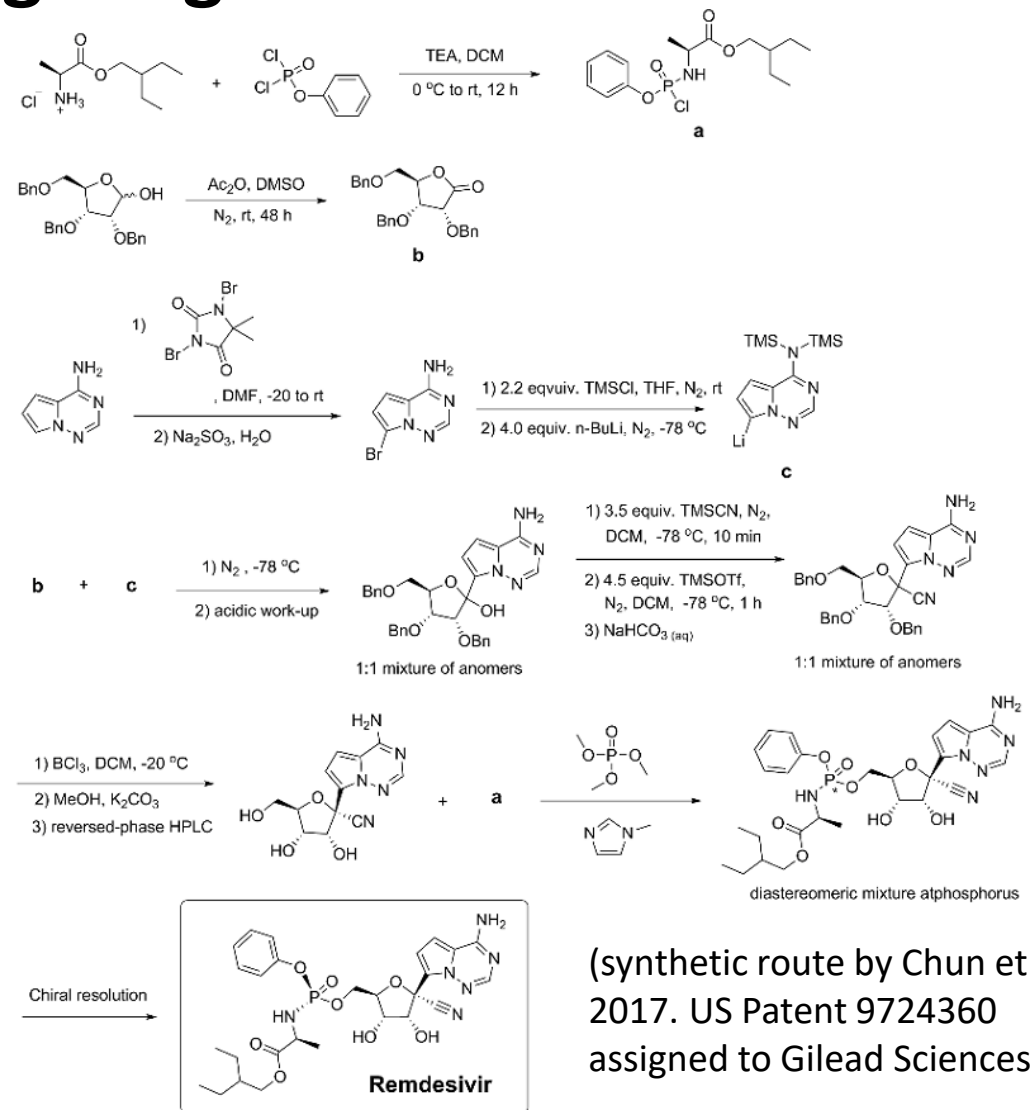
- BCG (Tuberculosis)

Surviving COVID-19: Repurposing drugs

Remdesivir



- Remdesivir was originally developed for Ebola and is a repurposed drug. It decreased COVID-19 hospital recovery time from 15 days to 11 days.
- Gilead says it may take 6 to 8 months to optimize the chemical synthesis process. Availability and cost are still undetermined. (C&E News, April 20, 2020).



(synthetic route by Chun et al., 2017. US Patent 9724360 assigned to Gilead Sciences Inc.)

Surviving COVID-19:
We need appropriate solutions for the Bottom of the Pyramid

Sci Dev Net

27/04/20

Build diverse food systems for post-COVID-19 world

Surviving COVID-19:
We must find our own solutions

Behavior

- Physical distancing
- Facemask
- Frequent handwashing
- Disinfection

Antibodies

- Own antibodies (COVID-19 survivors)
- Convalescent serum
- Monoclonal antibodies
- Vaccines

Therapeutics

- Repurposed drugs: Remdesivir, Hydroxychloroquine
- Traditional medicine, Ayurveda, TCM
- VCO

Immune system

- Vitamins esp. C, D; Zn, Se
- Diet & Nutrition
- Lifestyle
- Exercise
- Traditional medicine, Ayurveda, TCM
- VCO

- Diagnostics / testing
- Contact tracing / IT
- Epidemiology / Modelling
- Quarantine

- ONE HEALTH = Human Health + Environmental Health

Surviving COVID-19: GO COCONUTS!

- Coconuts support farmers
- Coconut trees are environmentally friendly
- Coconuts can be intercropped with other crops
- Coconuts can be directly consumed as nourishing food
- Coconuts can be processed into numerous food products
- Coconuts can be processed into numerous industrial products, eg, oleochemicals, building materials, fibers, nanocarbon
- The Coconut Tree is truly the ***Tree of Life***


KEEP
CALM
AND
GO
COCONUTS!