Combatting Lipid-Enveloped Viruses: PRRSV, PEDV, ASFV & Maybe Even Covid-19

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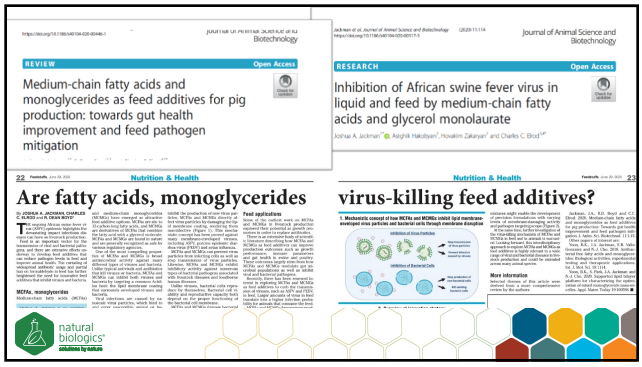

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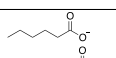
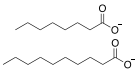
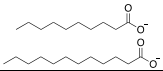
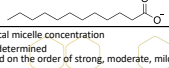
Overview of Medium-Chain Fatty Acids (MCFA)

	Compound Name (Molecular Formula)	Chemical Structure	Mol. Wt. (Da)	Melt. Point (°C)	CMC[1] (μM)	Smell[3]
Fatty Acids	Caproic Acid ($C_6H_{12}O_2$)		116.2	-3.4	N.D.[2]	Strong
	Caprylic Acid ($C_8H_{16}O_2$)		144.2	16.5	N.D.	Mod.
	Capric Acid ($C_{10}H_{20}O_2$)		172.3	31.6	3500	Mild
	Lauric Acid ($C_{12}H_{24}O_2$)		200.3	43.8	900	Minor

[1] CMC – Critical micelle concentration
[2] N.D. – Not determined
[3] Smell ranked on the order of strong, moderate, mild or minor

Adapted from: Jackman, Boyd and Elrod. JASB. 2020

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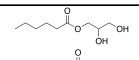
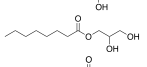
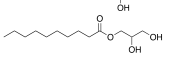
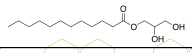
Overview of Medium-Chain Monoglycerides (MCMG)

	Compound Name (Molecular Formula)	Chemical Structure	Mol. Wt. (Da)	Melt. Point (°C)	CMC (μM)	Smell
Monoglycerides	Monocaproin ($C_9H_{18}O_4$)		190.2	19.4	N.D.	Minor
	Monocaprylin ($C_{11}H_{22}O_4$)		218.3	35.6	N.D.	Minor
	Monocaprin ($C_{13}H_{26}O_4$)		246.3	51.4	600	Minor
	Monolaurin ($C_{15}H_{30}O_4$)		274.4	62.5	60	Minor

Adapted from: Jackman, Boyd and Elrod, JASB, 2020

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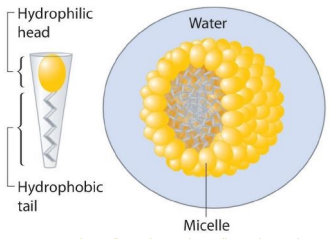
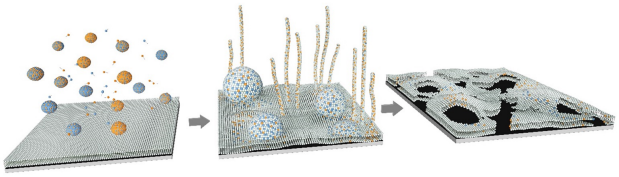
Critical Micelle Concentration is Key



5

Only above the CMC will MCFA or MCMG fuse with and affect membranes.



From: Yoon, et. al. JPCL, 2020.

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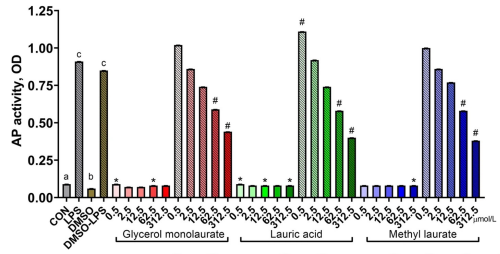
MCFA, MCMG, and analogues inhibit NFκβ



Mamedova, Elrod and Bradford, JASB, 2020

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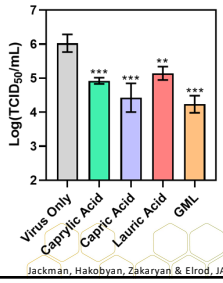
MCFA & GML have ASFV virucidal activity at 5 mM.



Jackman, Hakobyan, Zakaryan & Elrod, JASB, 2020, 11:114

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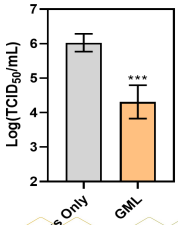
At 250 μM, only GML was virucidal against ASFV.



Jackman, Hakobyan, Zakaryan & Elrod, JASB, 2020, 11:114

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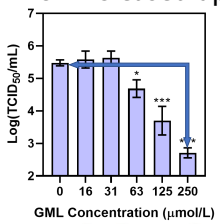
As low as 63 µM GML had ASFV antiviral activity which increased up to 250 µM



2.8 log reduction, 99.9% reduction in infectious virus

GML CMC = 60 uM

Jackman, Hakobyan, Zakaryan & Elrod, JASB, 2020, 11:114

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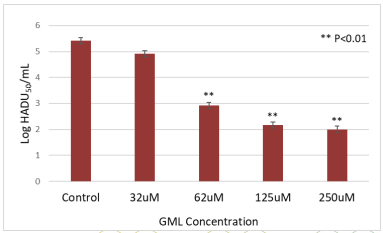
GML is also effective against wild-type ASFV.



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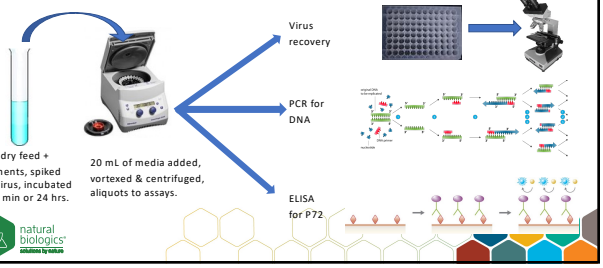
Antiviral Activity in Feed, Methods



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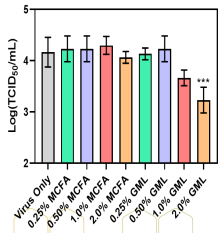
Only GML, at 2% in feed, with 30-minute exposure, had antiviral activity.



Jackman, Hakobyan, Zakaryan & Elrod, JASB, 2020, 11:114

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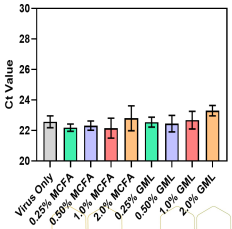
There were no effects on viral DNA levels.



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We used an ELISA to measure intact capsid p72 protein

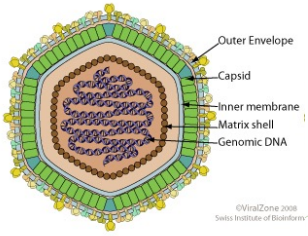

Image accessed from www.viralzone.expasy.org

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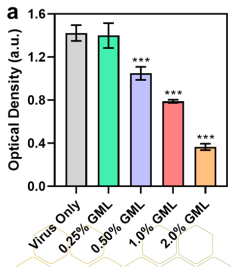
0.5% to 2% GML reduced intact p72 protein



Jackman, Hakobyan, Zakaryan & Elrod, JASB, 2020, 11:114

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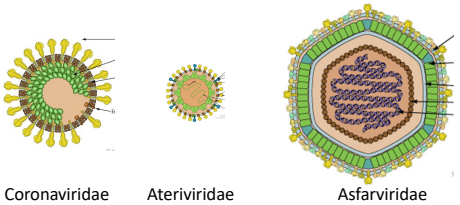
PEDV PRRSV ASFV SARS CoV-2



Coronaviridae	Ateriviridae	Asfarviridae	Coronaviridae
Alphacoronavirus	Alphaarterivirus	Asfivirus	Betacoronavirus
Single lipid env.	Single lipid env.	Double lipid env.	Single lipid env.
		Protein capsid	

Images accessed from www.viralzone.expasy.org

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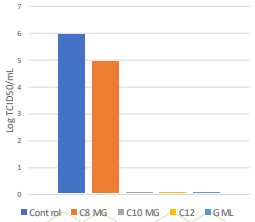
5 mM monocaprylin, lauric acid and GML are all highly antiviral against PRRSV



Elrod, Risley, Jackman & Diel, 2019, unpublished

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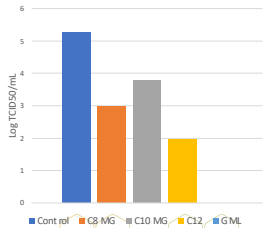
Only 5 mM GML completely inactivated PEDV



Elrod, Risley, Jackman & Diel, 2019, unpublished

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GML at 2 kg/ton of feed was effective at eliminating PRRS infection in Pipestone Challenge

	Control	GML
% Positive Feed	100%	33%
% Positive Oral	100% (Ct=26.1)	17% (Ct=33.0)
% Positive Serum	100%	0%
% Positive Pens (clinical signs)	100%	0%
ADG (lbs.)	0.44	1.1

Data used with permission of Berg & Schmidt

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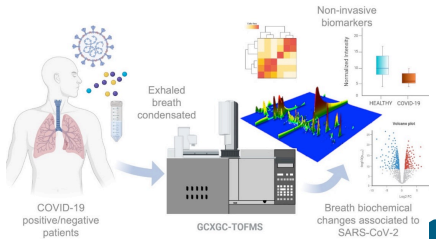
Metabolomics of exhaled breath in healthy and COVID-19 subjects



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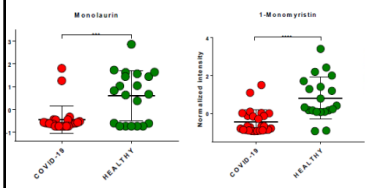
Healthy subjects could be differentiated by the presence of GML and monomyristate



- "…an abundance of EBC fatty acids can be used to discriminate COVID-19 patients and that they may have a protective effect, thus suggesting their potential use as a preventive strategy against the infection."

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Summary

- MCFA and GML had ASF virucidal activity at 5 mM
  - Resulting in 1.1 to 1.7 log reduction in viral load
- GML was active at 250 µM, about 20x more potent
  - 2.8 log reduction in total antiviral activity
    - 1.7 log reduction attributable to virucidal activity
    - ~1.1 log reduction presumably through another mechanism
    - Disruption of P72 protein may inhibit fusion with host cells

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Summary

- In feed, only GML was active against ASFV at the inclusion rates tested
  - Resulting in a 0.94 log reduction @ 30 minutes when compared to control
- None of the treatments affected the presence of viral DNA in feed

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Summary

- GML significantly disrupted the major capsid protein present in ASFV.
- This may explain why GML demonstrated activity beyond virucidal, perhaps interfering in fusion with or replication within host cells

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Summary

- Monocaprylin, lauric acid and GML eliminated PRRSV *in vitro.*
- Only GML completely eliminated PEDV *in vitro.*
- GML significantly reduced PRRSV in feed, oral fluids and serum of pigs at 2 kg/ton of feed.
- GML eliminated clinical signs of PRRSV in virus-challenged pigs and improved ADG.

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Conjecture

- GML and monomyristate (C14 monoglyceride) were present in breath of healthy subjects when compared to that of COVID-19 patients.
- SARS CoV-2, a lipid enveloped virus, would likely be susceptible to disruption by GML.
- Presence of GML in respiratory mucosa suggests circulation of this potent antimicrobial, antiviral and anti-inflammatory compound which may be protective.

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- Acknowledgements
  - Dr. Joshua Jackman, Sungkyunkwan University
  - Dr. Hovakim Zakaryan, Armenia National Academy of Science
  - Dr. Dean Boyd, Animal Nutrition Research
  - Dr. Diego Diel, Cornell University
  - Dr. Chad Risley, Berg & Schmidt

- Any omissions or mistakes are solely my own. You can let me know about them, or start a discussion about this work at: celrod@naturalbiologics.com

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