Lessons from COVID-19: Potential for botanical-based remedies

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SOUTHWEST COLLEGE OF NATUROPATHIC MEDICINE & HEALTH SCIENCES

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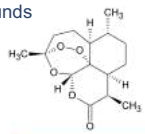
Why Botanicals?

- Distributed worldwide (including developing countries):
  - Low-cost production
  - Stability
- Ease of administration
- Natural alternative to pharmaceuticals
- Potential isolation of novel active compounds



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How can botanicals treat human diseases?

?

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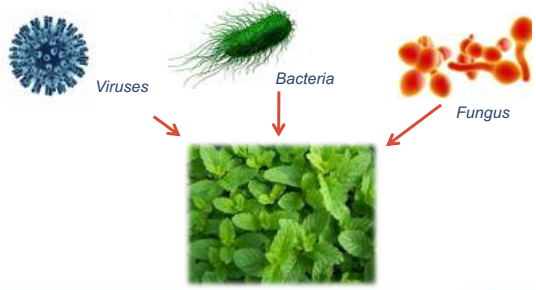
Plants are also susceptible to microbial infections:



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Plants are also susceptible to microbial infections:

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Evaluation of botanicals in a laboratory environment: Evidence-based medicine

Cell culture systems

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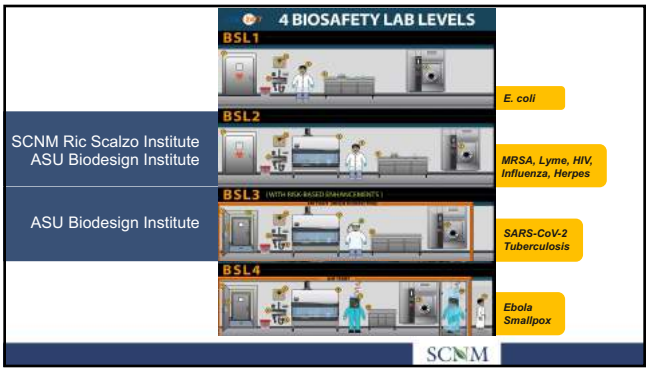
4 BIOSAFETY LAB LEVELS
BSL1
BSL2
BSL3
BSL4
E. coli
MRSA, Lyme, HIV, Influenza, Herpes
SARS-CoV-2 Tuberculosis
Ebola Smallpox
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Working with SARS-CoV-2 at the ASU Biodesign BSL3 facility
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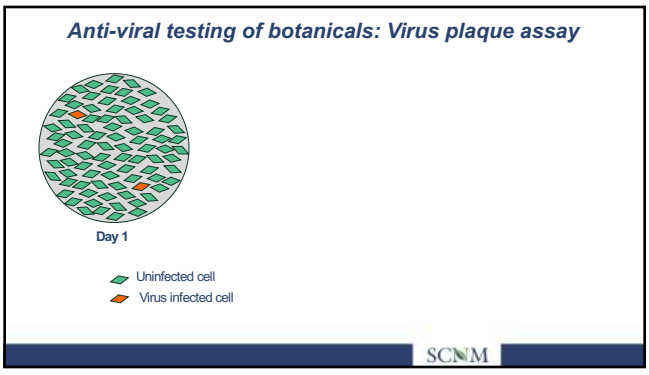
Anti-viral testing of botanicals: Virus plaque assay
Day 1
Uninfected cell
Virus infected cell
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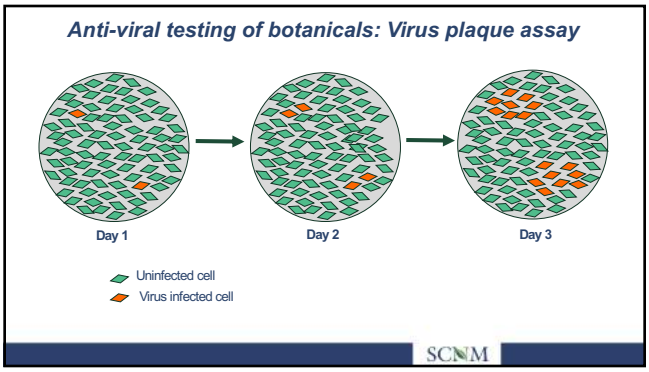
Anti-viral testing of botanicals: Virus plaque assay
Day 1
Day 2
Day 3
Uninfected cell
Virus infected cell
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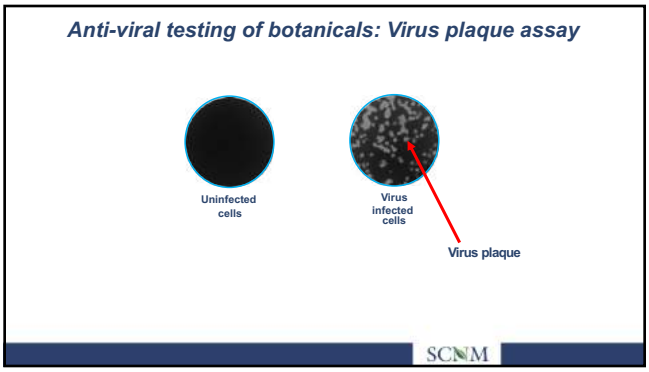
Anti-viral testing of botanicals: Virus plaque assay
Uninfected cells
Virus infected cells
Virus plaque
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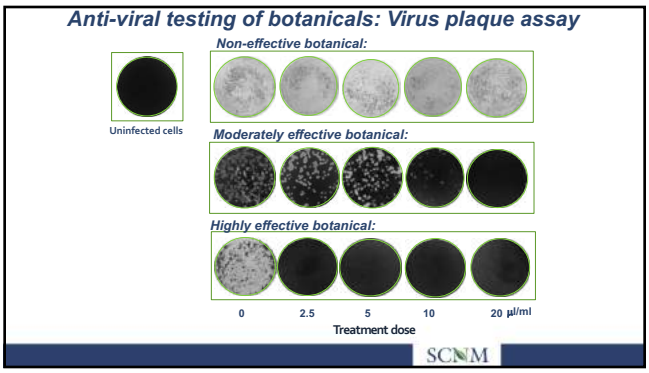
Anti-viral testing of botanicals: Virus plaque assay
Uninfected cells
Non-effective botanical:
Moderately effective botanical:
Highly effective botanical:
0
2.5
5
10
20 µl/ml
Treatment dose
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Botanical extracts being tested against SARS-CoV-2:

Botanical	Common name	Part used
Angelica keiskei	Ashitaba	Leaf
Artemisia annua	Sweet wormwood, Qing Hao	Aerial
Broussonetia papyrifera	Paper mulberry	Fruit
Bupleurum falcatum	Bei Chai Hu	Root
Camellia sinensis	Green tea	Leaf
Chrysanthemum indicum	Yellow chrysanthemum, Ju Hua	Flower
Cinnamomum cassia	Cinnamon	Bark
Cistus reticula	Tangerine peel	Fruit peel
Coptis chinensis	Goldthread	Root
Forsythia suspensa	Goldenbell, You Ji Lian Qiao	Fruit
Glycyrrhiza glabra	Licorice	Root
Glycyrrhiza uralensis	Asian Licorice, Gan Cao	Root
Houttuynia cordata	Fish leaf, Yu Xing Cao	Leaf
Isatis indigotica	Woad, Wild indigo, Da Qing Ye	Leaf
Lonicera japonica	Japanese honeysuckle	Flower
Melissa officinalis	Lemon balm	Leaf
Mentha haplocalyx	Wild mint, Bo He	Leaf
Morus alba	Mulberry, Sang Ye	Leaf
Phragmites communis	Reed, Lu Gen	Root
Platycodon grandiflorus	Balloon flower, You Ji Jie Geng	Root
Polygonum cuspidatum	Japanese Knotweed, You Ji Hu Zhang	Root
Polygonum multiflorum	Shou wu wan	Root
Prunus armeniaca	Bitter apricot, You Ji Xu Xing	Kernel
Radix polygoni	He Shou Wu	Root
Rheum palmatum	Rhubarb, You Ji Da Huang	Root
Salvia miltiorrhiza	Chinese sage, You Ji Dan Shen	Root
Saposhnikovia divaricata	Fang Feng	Root
Scutellaria baicalensis	Chinese skullcap, You Ji Huan Qin	Root
Sophora flavescens	Ku Shen	Root
Urtica dioica	Stinging nettle	Leaf
Zingiber officinale	Ginger	Root

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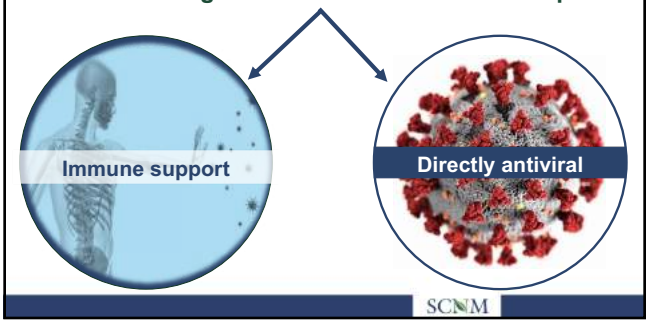
Potential Targets for Botanical-Based Therapies



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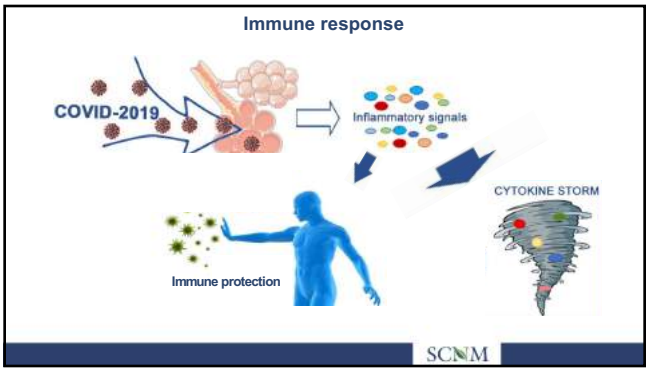
Immune response
COVID-2019
Inflammatory signals
CYTOKINE STORM
Immune protection
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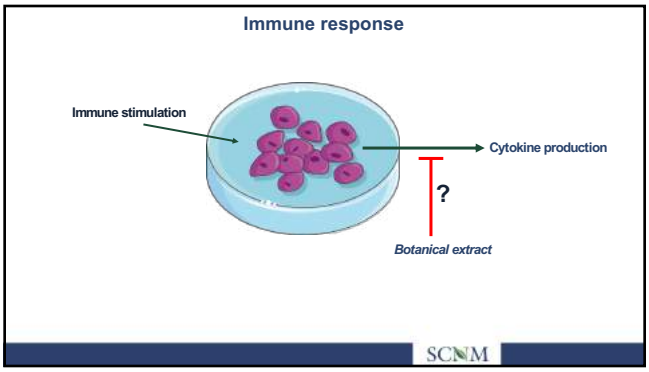
Immune response
Immune stimulation
Cytokine production
?
Botanical extract
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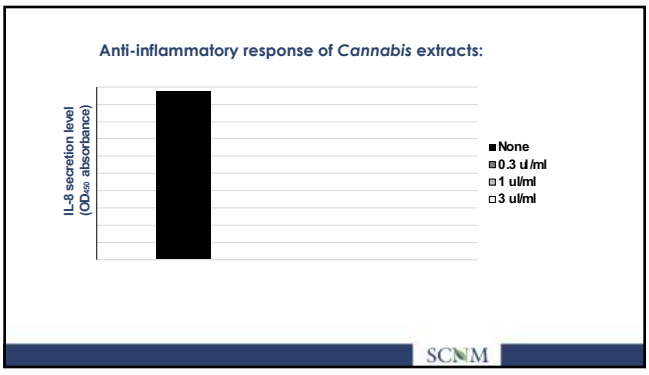
Anti-inflammatory response of Cannabis extracts:
IL-8 secretion level (OD450 absorbance)
None
0.3 ul/ml
1 ul/ml
3 ul/ml
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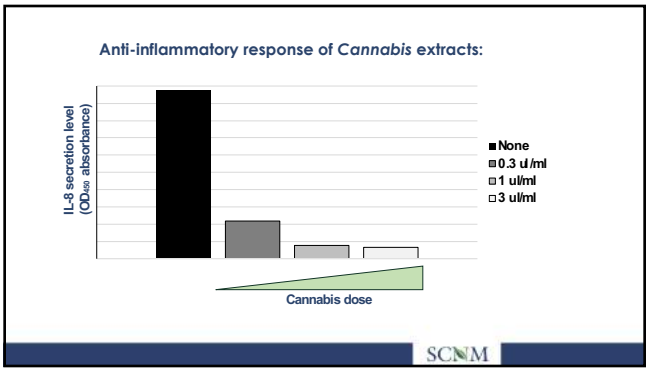
Anti-inflammatory response of Cannabis extracts:
IL-8 secretion level (OD450 absorbance)
None
0.3 ul/ml
1 ul/ml
3 ul/ml
Cannabis dose
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Testing botanical safety:
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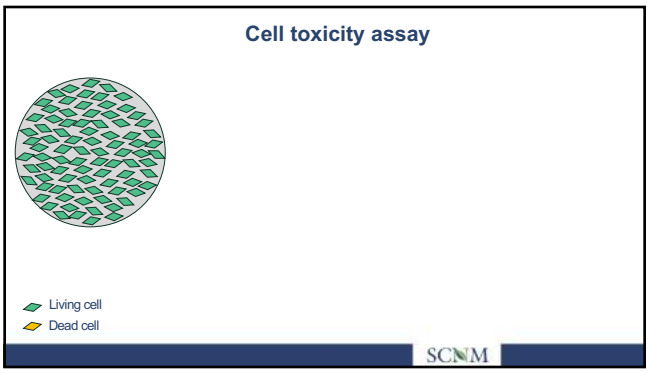
Cell toxicity assay
Living cell
Dead cell
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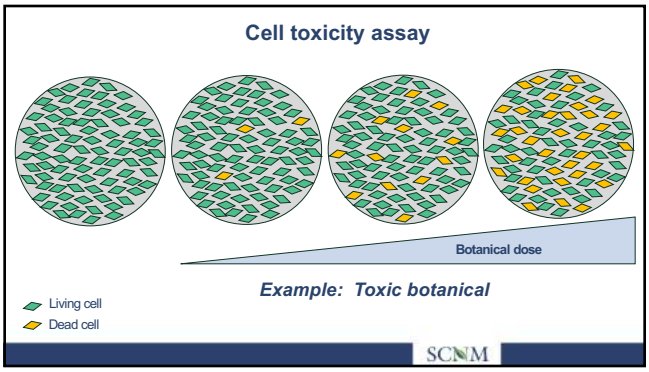
Cell toxicity assay
Botanical dose
Example: Toxic botanical
Living cell
Dead cell
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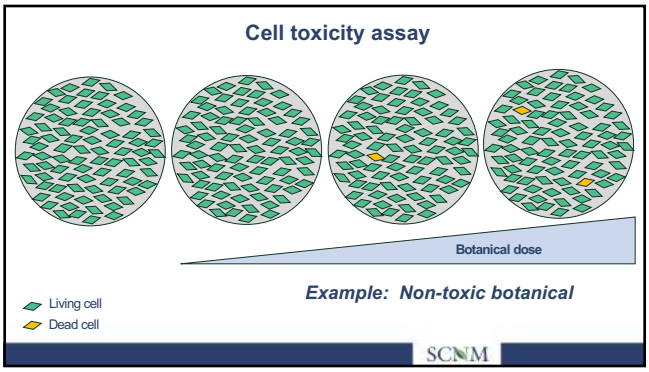
Cell toxicity assay
Botanical dose
Example: Non-toxic botanical
Living cell
Dead cell
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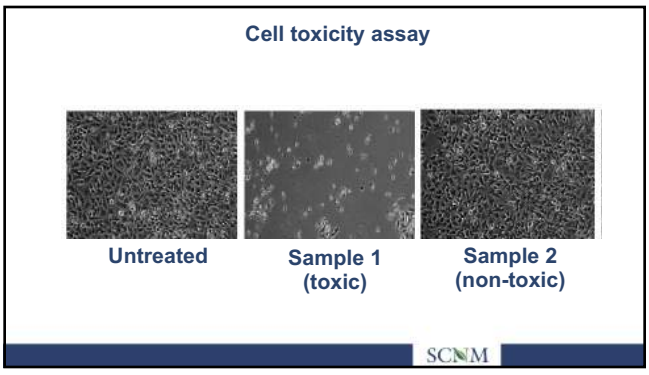
Cell toxicity assay
Untreated
Sample 1 (toxic)
Sample 2 (non-toxic)
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Selectivity Index (SI) = $\frac{\text{cell toxicity dose}}{\text{viral inhibition dose}}$

The higher the SI ratio, the theoretically **more effective and safe** a drug would be during *in vivo* treatment for a given viral infection.

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Top anti-SARS-CoV-2 botanicals:

Botanical	Cell toxicity (ul/ml)	Virus inhibition (ul/ml)	Selectivity Index
Houttuynia cordata	40	3	>13
Scutellaria baicalensis	10-20	1-3	7
Chrysanthemum indicum	20	2-5	6
Camellia sinensis	12	2	6
Salvia miltiorrhiza	60	1	60

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Botanical synergism
Understanding the mechanism of action:

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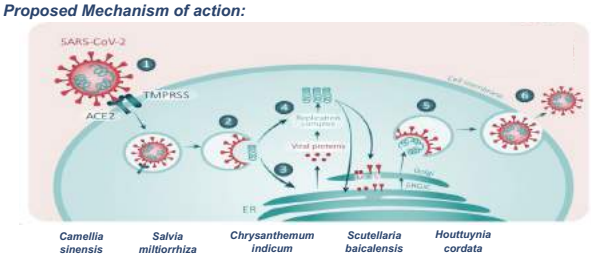
Proposed Mechanism of action:



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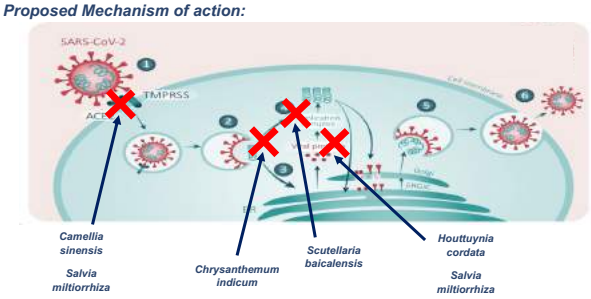
Proposed Mechanism of action:



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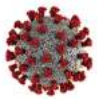
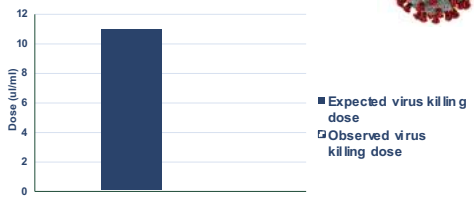
Synergistic effects
Anti-SARS-CoV-2 activity of botanical blend:





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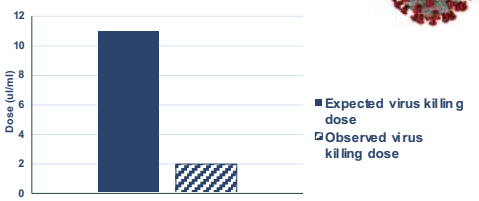
Synergistic effects
Anti-SARS-CoV-2 activity of botanical blend:



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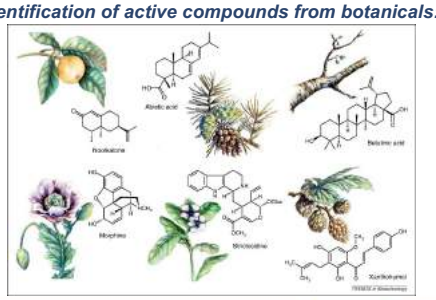
Identification of active compounds from botanicals:



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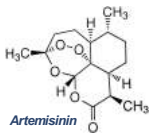
Artemisia annua:



Artemisinin

Used to treat malaria

Discovery of artemisinin and its antimalarial properties by the Chinese scientist, Tu Youyou, led to award of the 2015 Nobel Prize in Physiology or Medicine

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Anti-coronavirus activity of Artemisia and Artemisinin:

Treatment	Cell toxicity (ul/ml)	Virus inhibition (ul/ml)	Selectivity Index
Artemisia annua	25 ul/ml	3 ul/ml	8

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Anti-coronavirus activity of Artemisia and Artemisinin:

Treatment	Cell toxicity (ul/ml)	Virus inhibition (ul/ml)	Selectivity Index
Artemisia annua	25 ul/ml	3 ul/ml	8
Artemisinin	250 uM	5 uM	50

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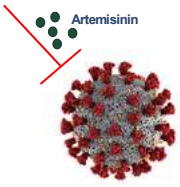
Anti-coronavirus activity of Artemisia and Artemisinin:

Artemisia annua



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New and effective therapies lie within our reach with what nature has already created.
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Q & A

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