Fungi, the two sides of the same coin

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Beneficial Aspects of Fungi

Microorganisms are known as important sources of natural compounds that have been studied and applied for different purposes in distinct areas. Specifically, in the pharmaceutical area, fungi have been explored mainly as sources of antibiotics, antiviral, anti-inflammatory, enzyme inhibitors, hypercholesteremic, anticancer, immunomodulators, and immunosuppressants agents.

Some Fungal metabolites that have been developed into pharmaceutical products

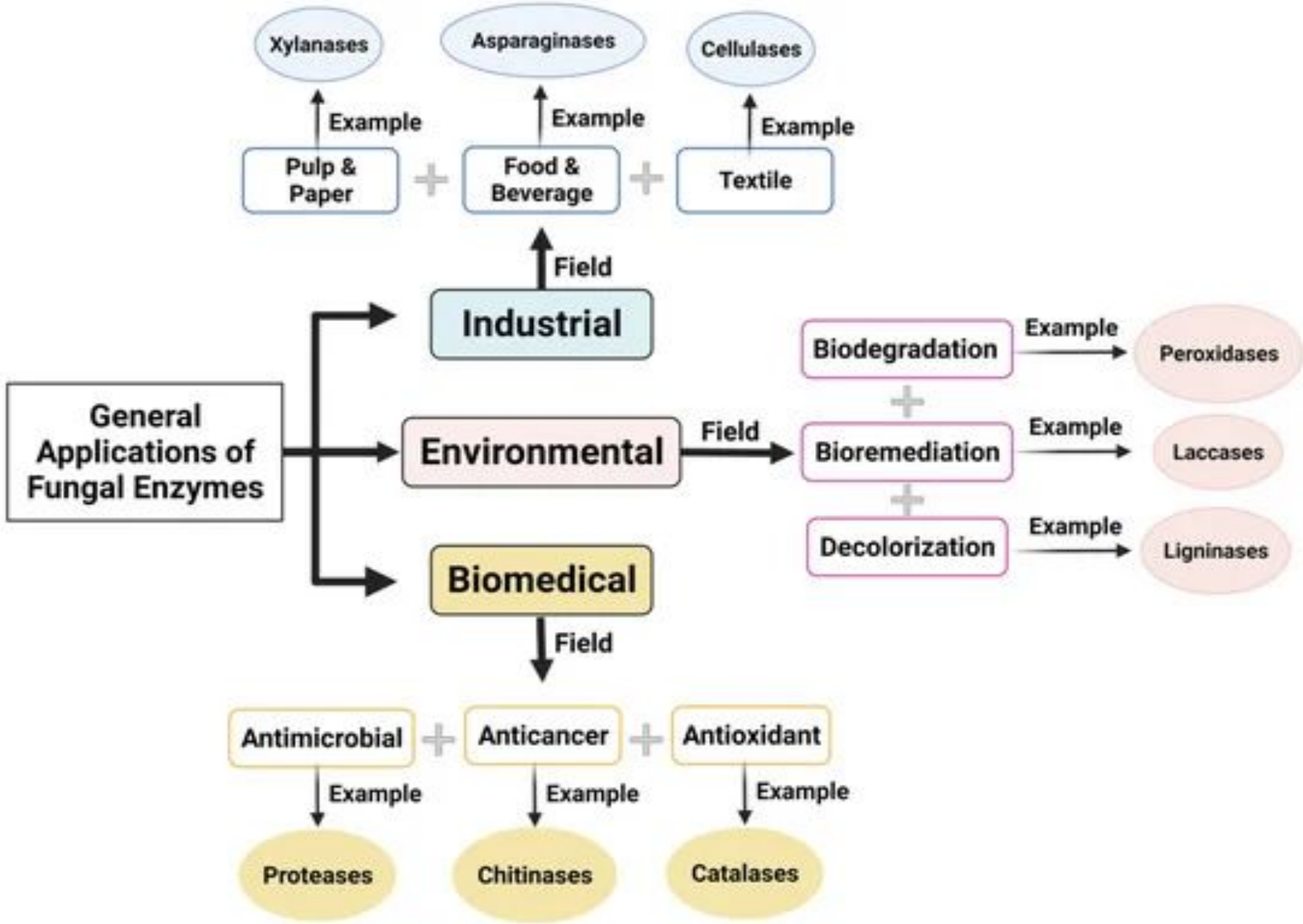
Metabolite	Source species	Indication(s)
Penicillins G and V	*Penicillium rubens, Penicillium chrysogenum*	Gram-positive and some Gram-negative bacteria
Cephalosporin C	*Acremonium chrysogenum*	Gram-positive and some Gram-negative bacteria
Fusidic acid	*Acremonium fusidioides*	Topical antibiotic for Gram-positive bacterial infections
Griseofulvin	*Penicillium griseofulvum,* and *other Penicillium spp.*	Treatment of fungal infections of the skin, hair, and nails
Cyclosporin A	*Tolypocladium inflatum*	Prevention of organ transplant and tissue graft rejection
Ergotamine	*Claviceps purpurea, Claviceps fusiformis,* and *Claviceps paspali*	Vasoconstrictor used as antimigraine agent, also combined with belladonna and phenobarbital for relief from menopausal hot flashes
Ergometrine (ergonovine)	*C. purpurea, C. fusiformis,* and *C. paspali*	Treatment of postpartum hemorrhage

Beneficial Aspects of Fungi

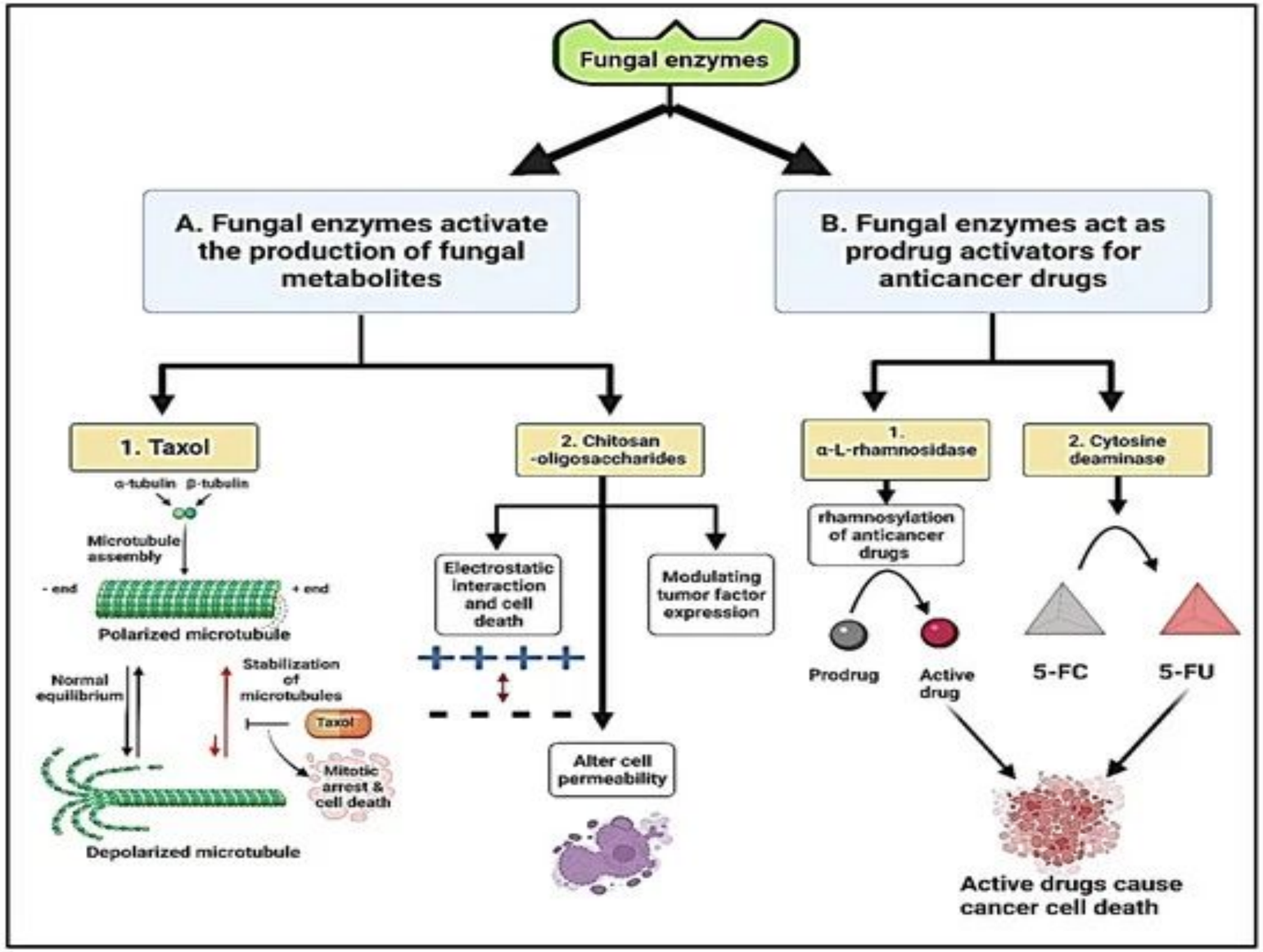
Currently, fungal enzymes are accounted for more than 50% of the total enzymes market. This huge market share is largely attributed to a few species of *Aspergillus*, *Trichoderma*, *Rhizopus*, and *Penicillium* genera that fulfill the commercial-scale requirements for enzymes production.

Recently, mushroom cultivation has represented a promising competitor in enzymes production in terms of higher productivity and lower invested cost.

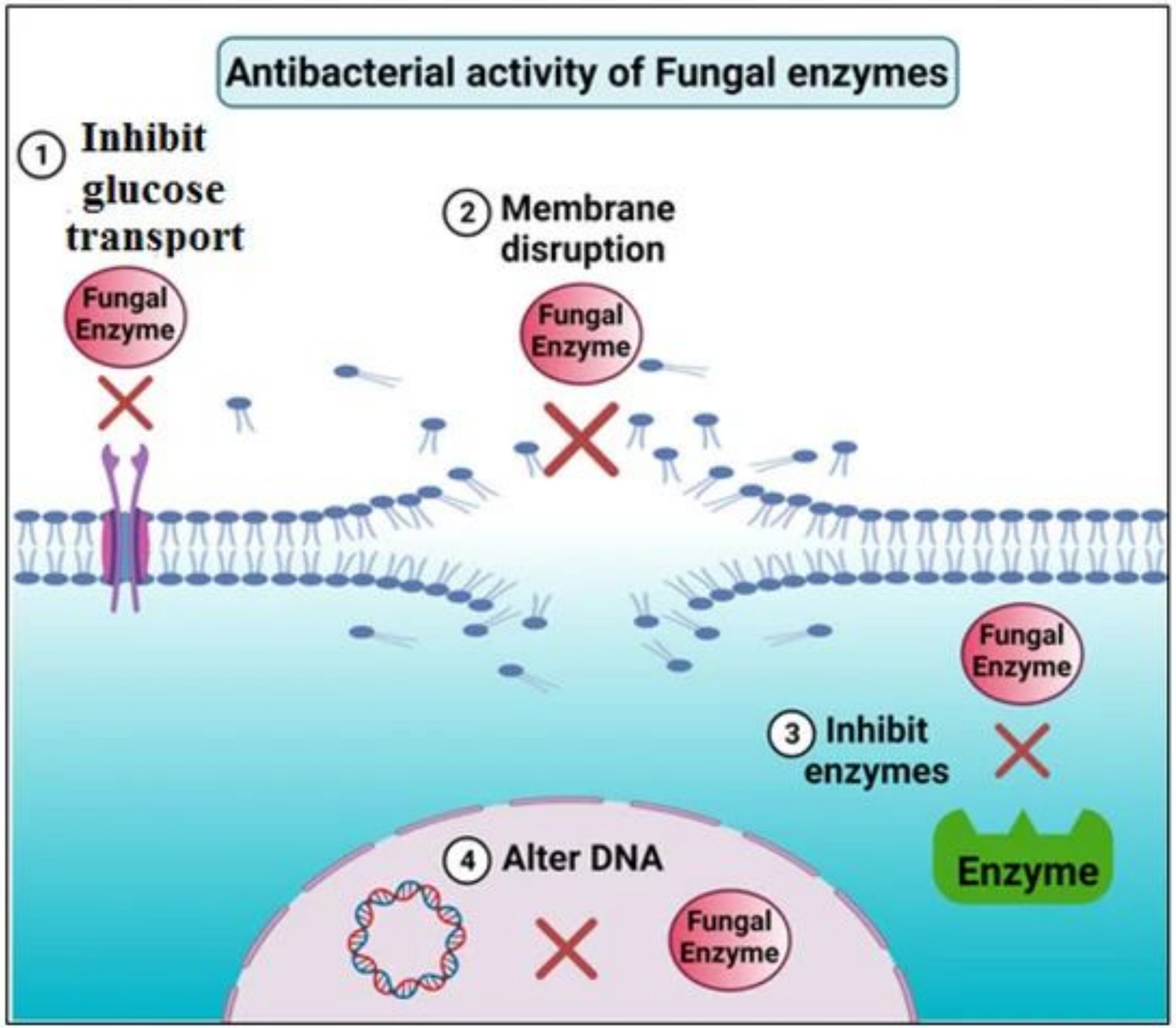
Fungal Proteins as small bioactive molecules



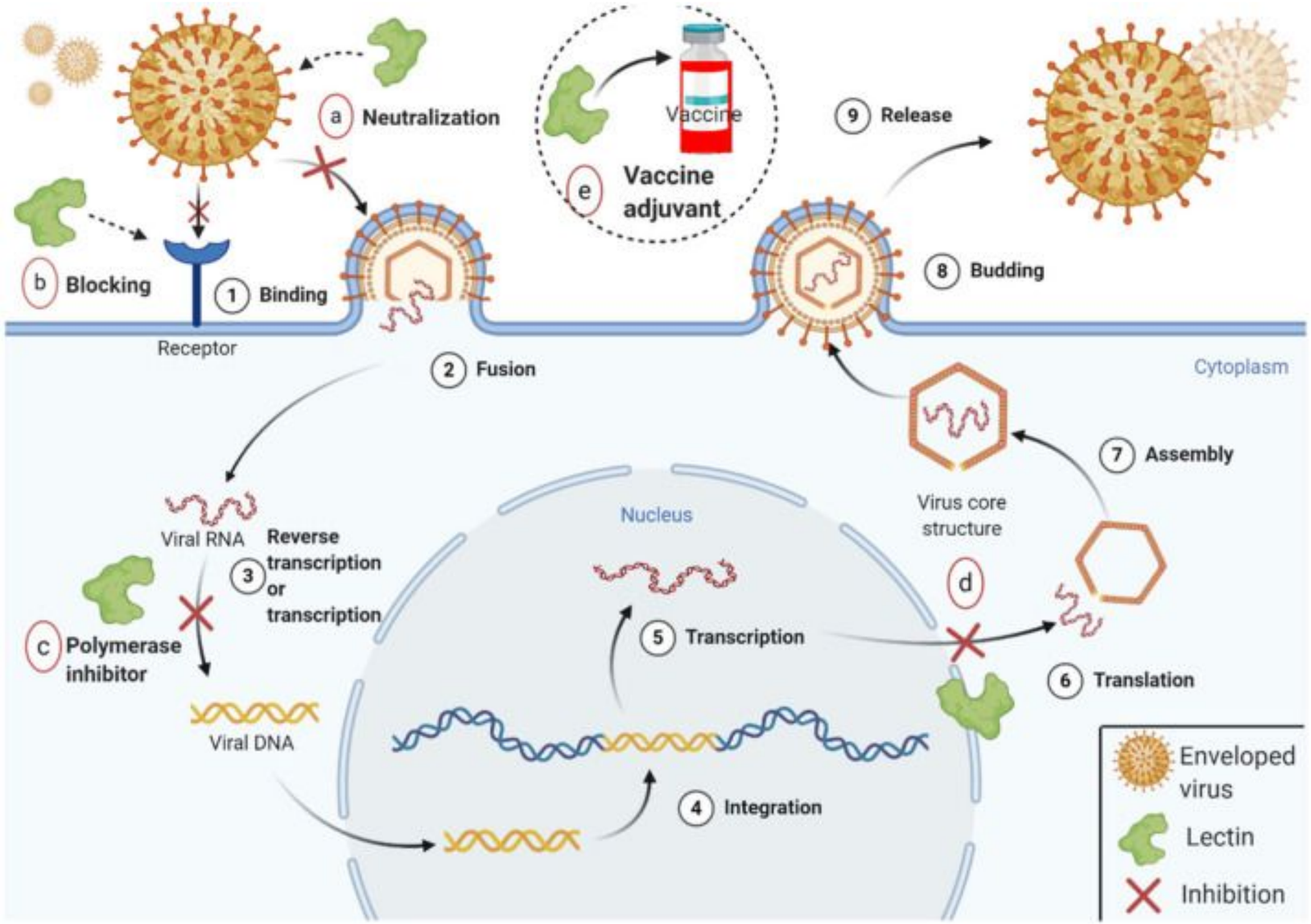
Fungal Proteins Anticancer activity



Fungal Proteins Antibacterial activity



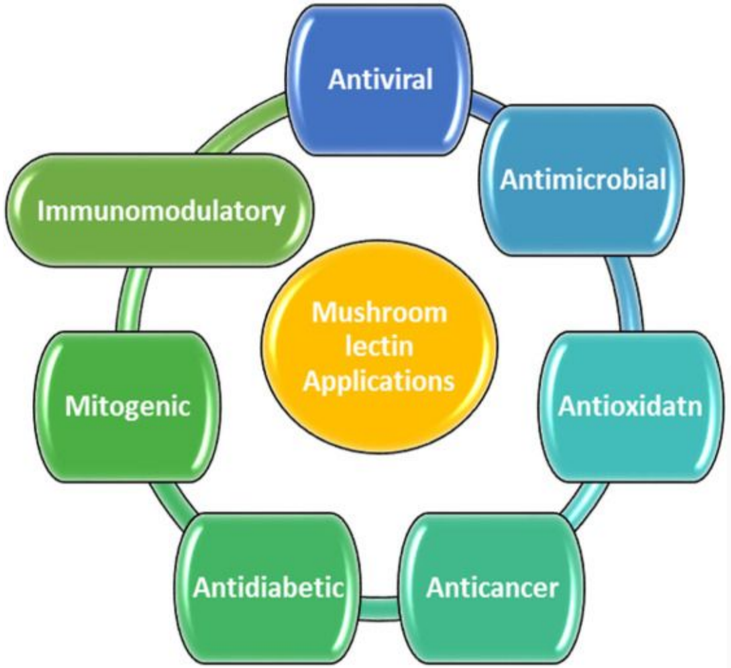
Fungal Proteins Antiviral activity



Fungal Lectins Antiviral activity

Lectin is one of the most studied carbohydrate-binding proteins from mushroom. About 82% of fungal lectins have been reported from mushrooms, 15% from molds and 3% from yeasts

Lectins are oligomeric widely investigated proteins with unique molecular and physiological characteristics, including diversity in structure, molecular size, metal requirements, glycosylation and carbohydrate specificity.



In vitro Assessment of the Antiviral Activity of Lectin Extracted from *Pleurotus ostreatus* Mushroom against Herpes Simplex Virus and Hepatitis B virus Infection

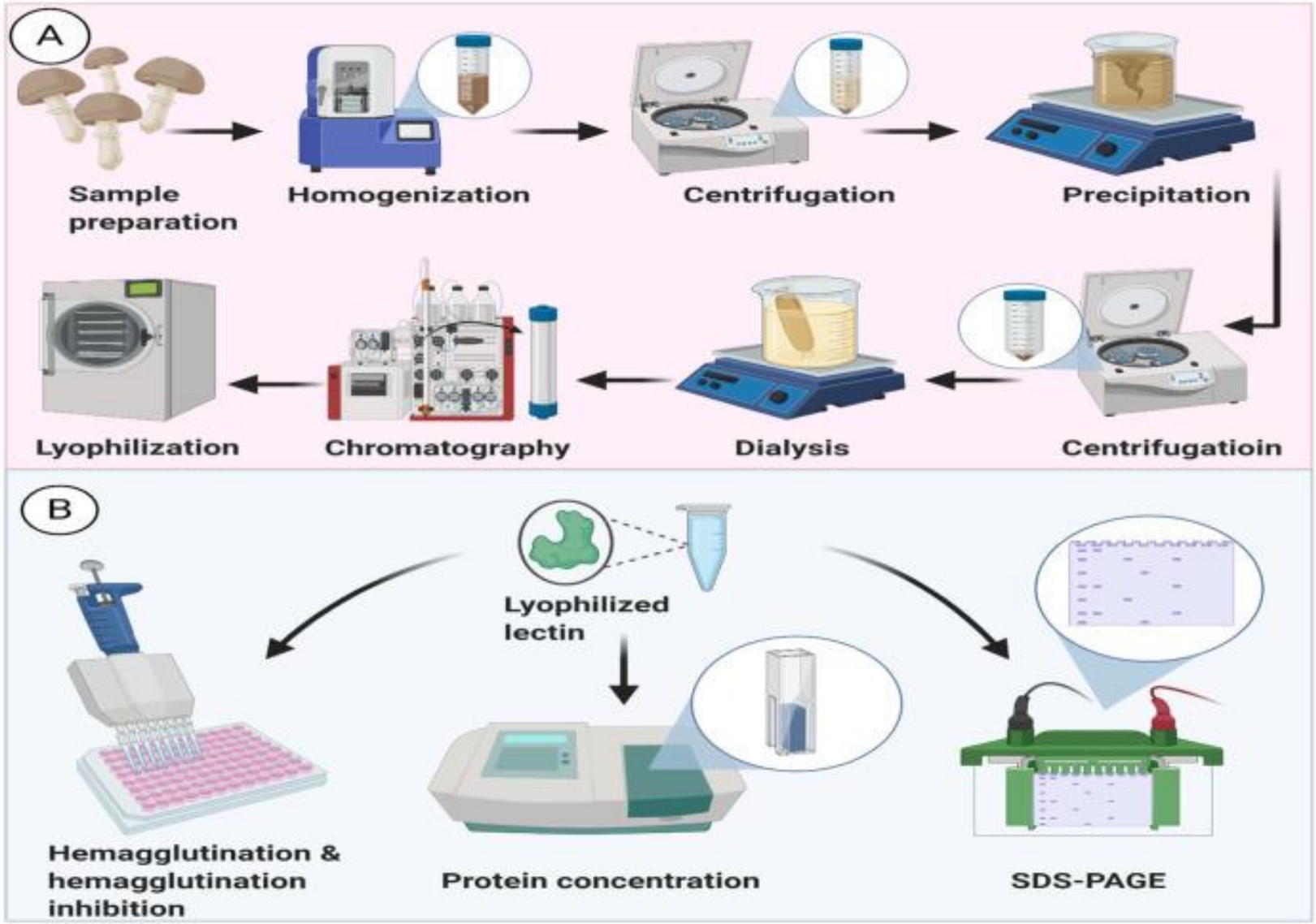
- **Lectins could be used as broad-spectrum antiviral agents rather than the ‘one bug–one drug’ approach.**

Purification and characterization

Assessment of the cytotoxic effect

Detection of the antiviral activity

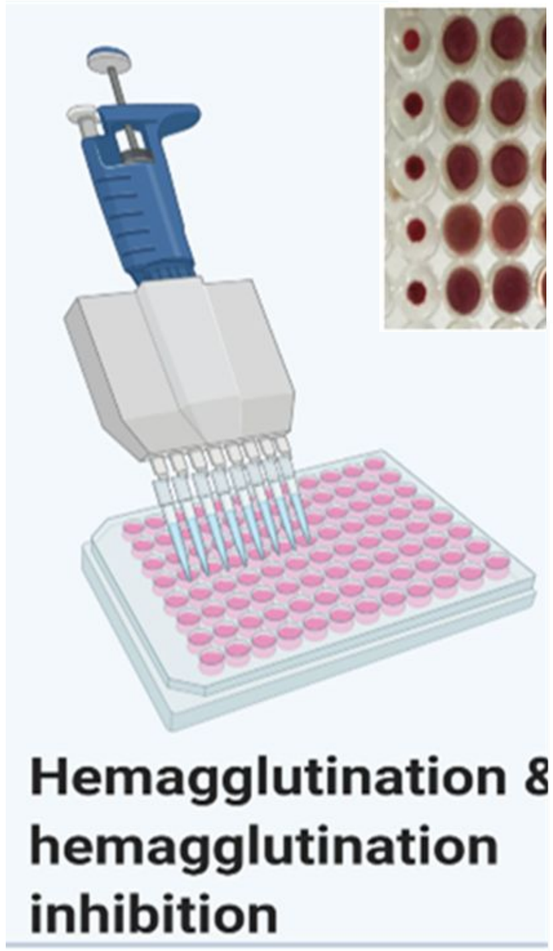
Mushroom lectins and its Antiviral activity

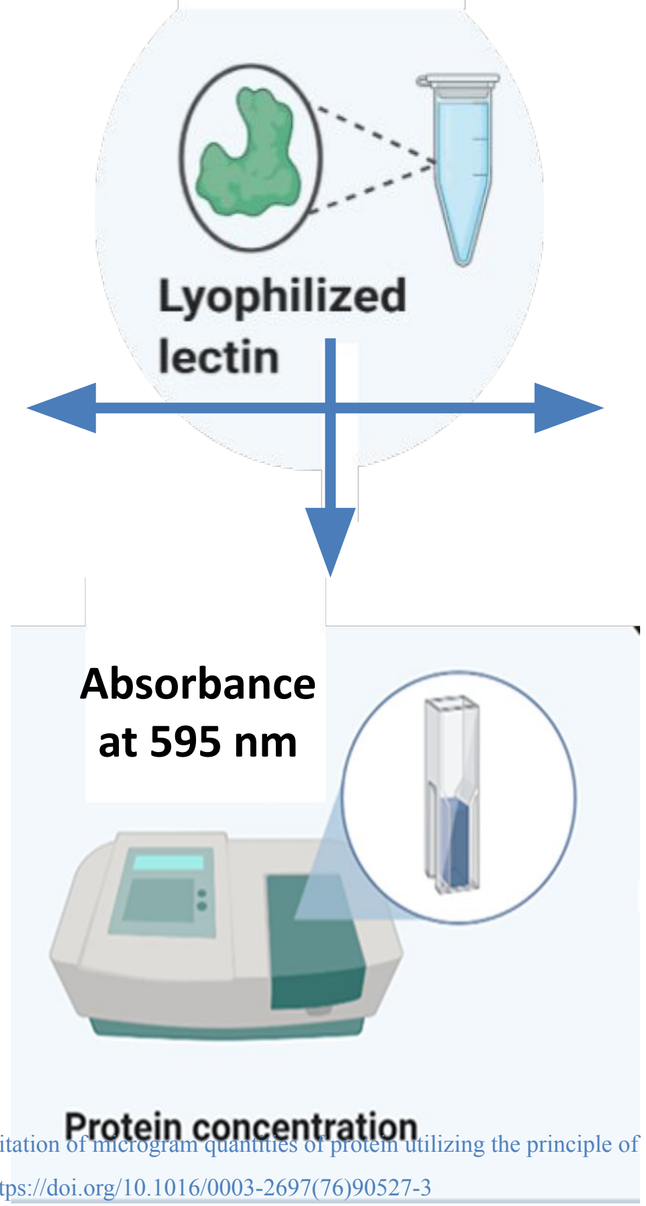


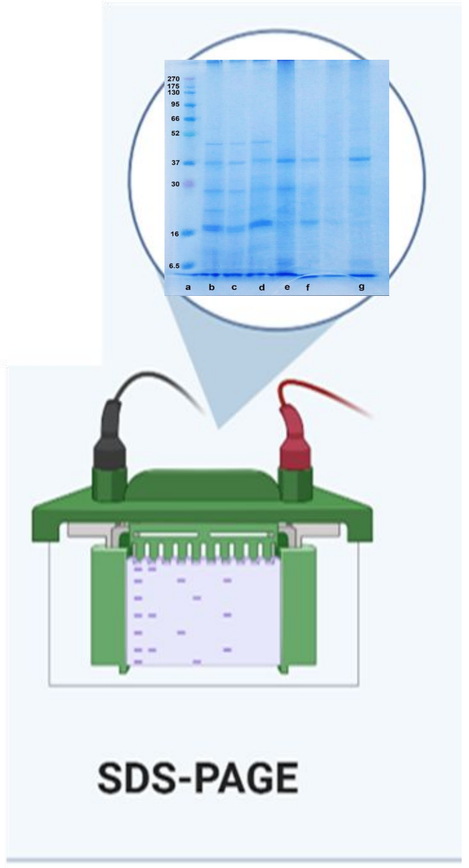
A

Sample preparation

B) Characterization of lectin







Bradford, M. M. (1976). A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. *Analytical Biochemistry*, *72*(1–2), 248–254. https://doi.org/10.1016/0003-2697(76)90527-3

The characteristic features of the purified lectin (POL)

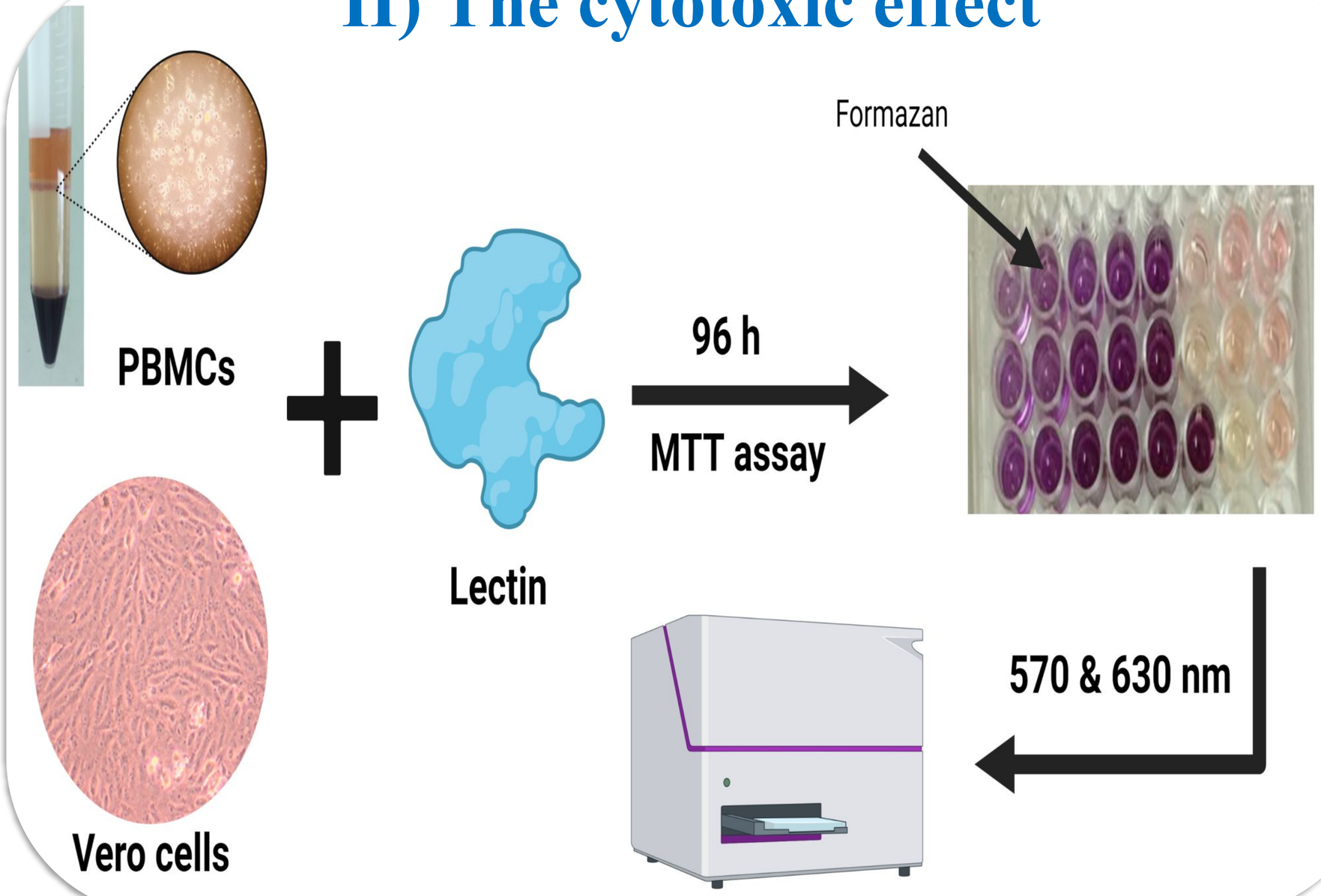
Purified lectin	Molecular weight (kDa)		HA (HU/ml)	pH stability	Thermostability (°C)	HAI
	SDS-PAGE	Native				
POL	39	80	Human O (4096)	4-9	Up to 40 °C	Fetuin and melibiose

Purification and characterization

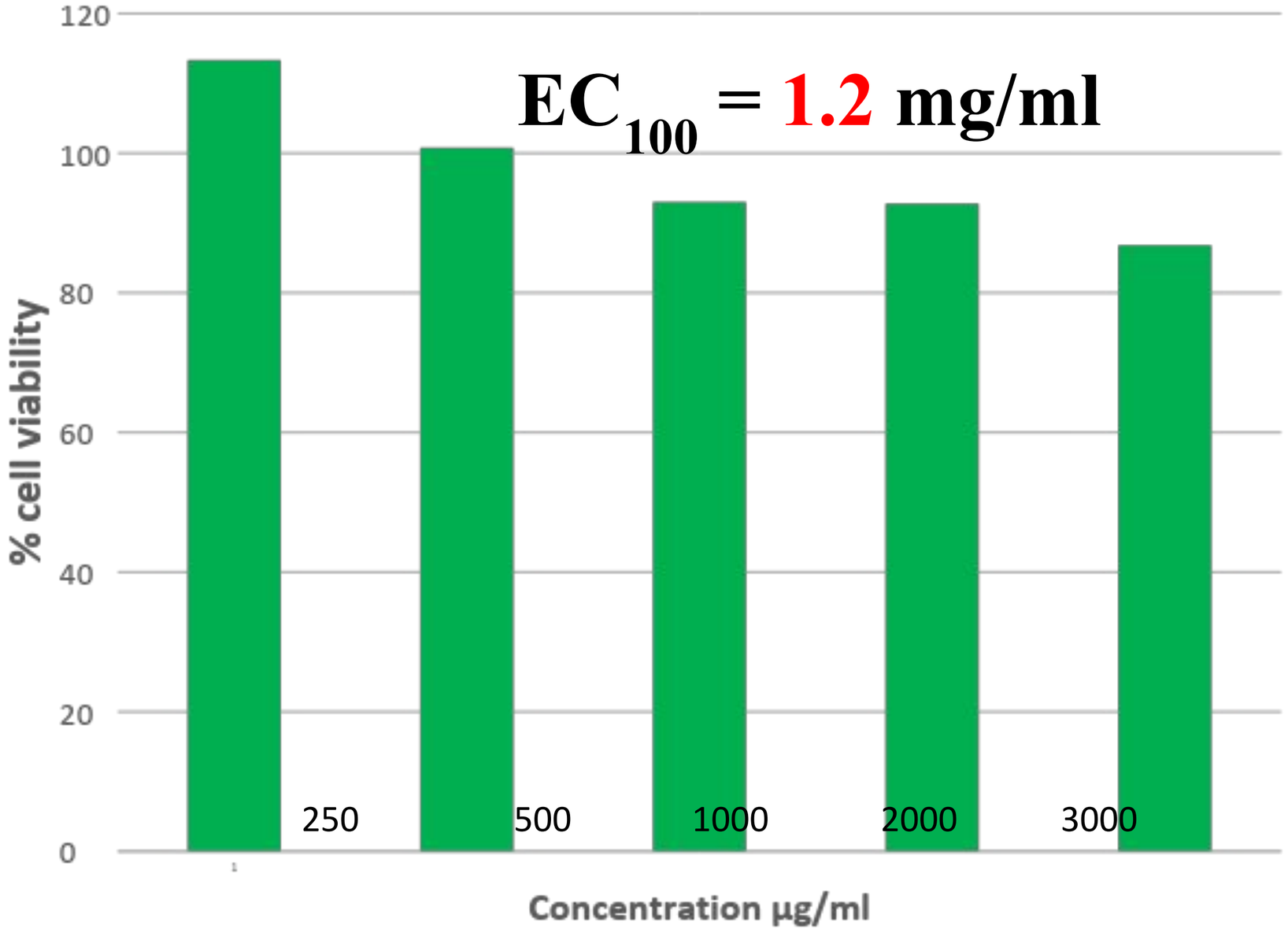
Assessment of the cytotoxic effect

Detection of the antiviral activity

II) The cytotoxic effect



II) The cytotoxic effect

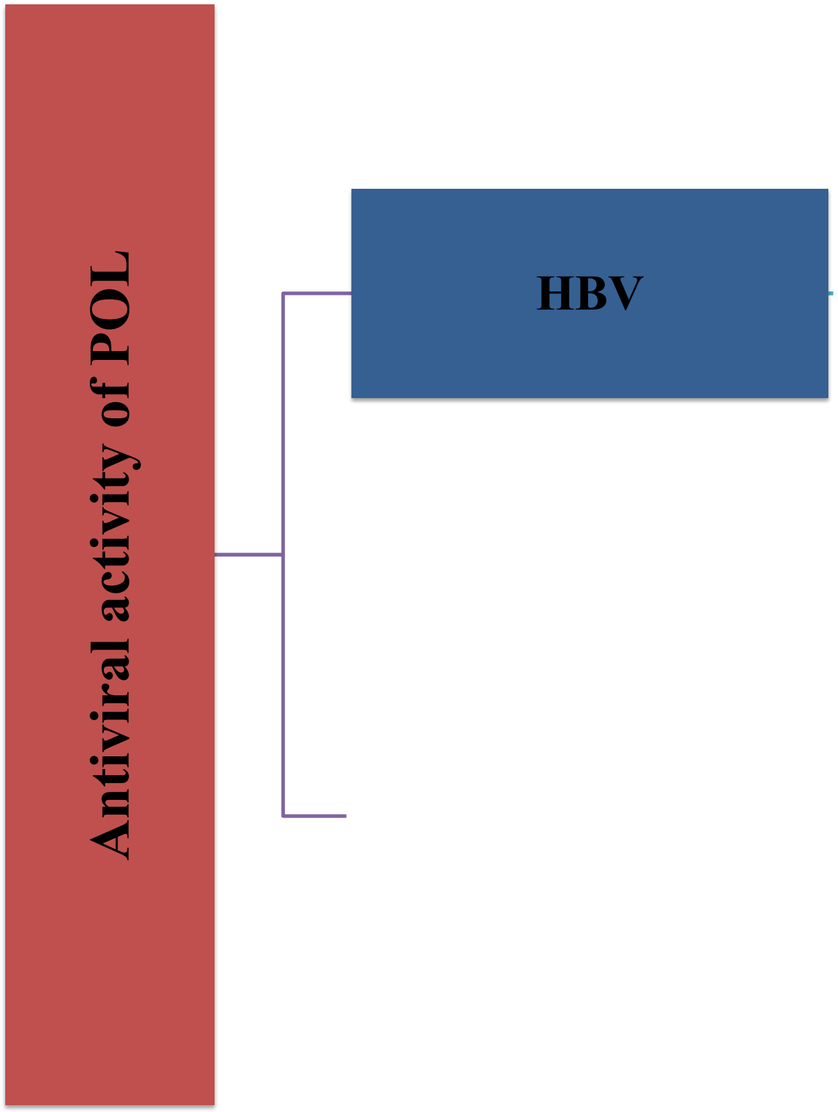


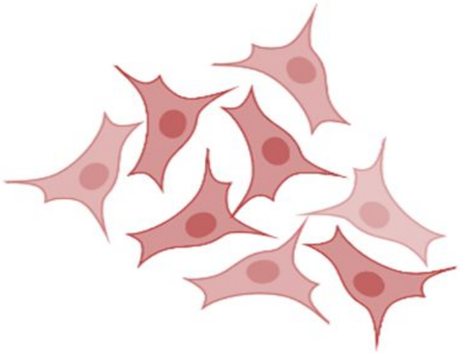
Purification and characterization

Assessment of the cytotoxic effect

Detection of the antiviral activity

III) *In vitro & in silico* detection of antiviral activity of POL

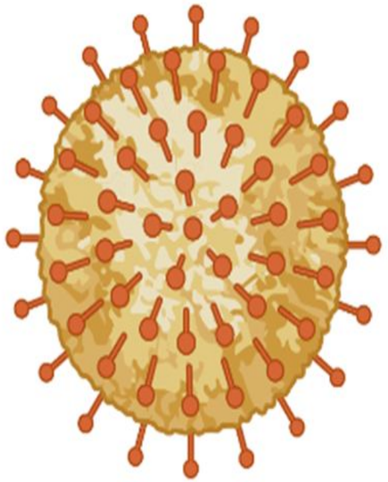

Antiviral activity of POL
HBV



Cell line

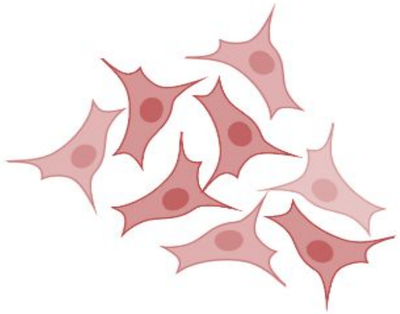
2 hours

Lectin



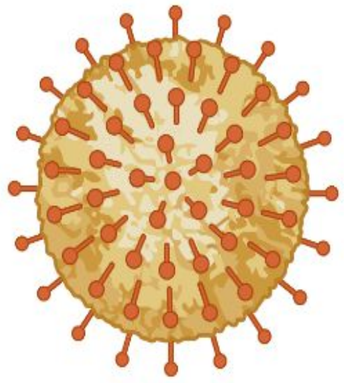
Virus

1- Investigation of the anti-HBV modes of action of lectins



Cell line

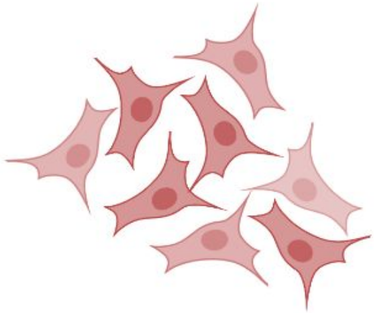
HepG2



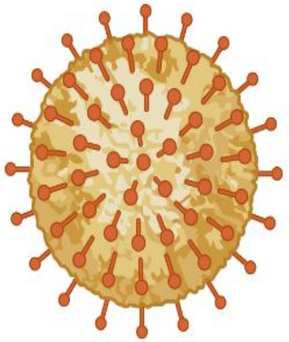
Virus

HBV

Treatment

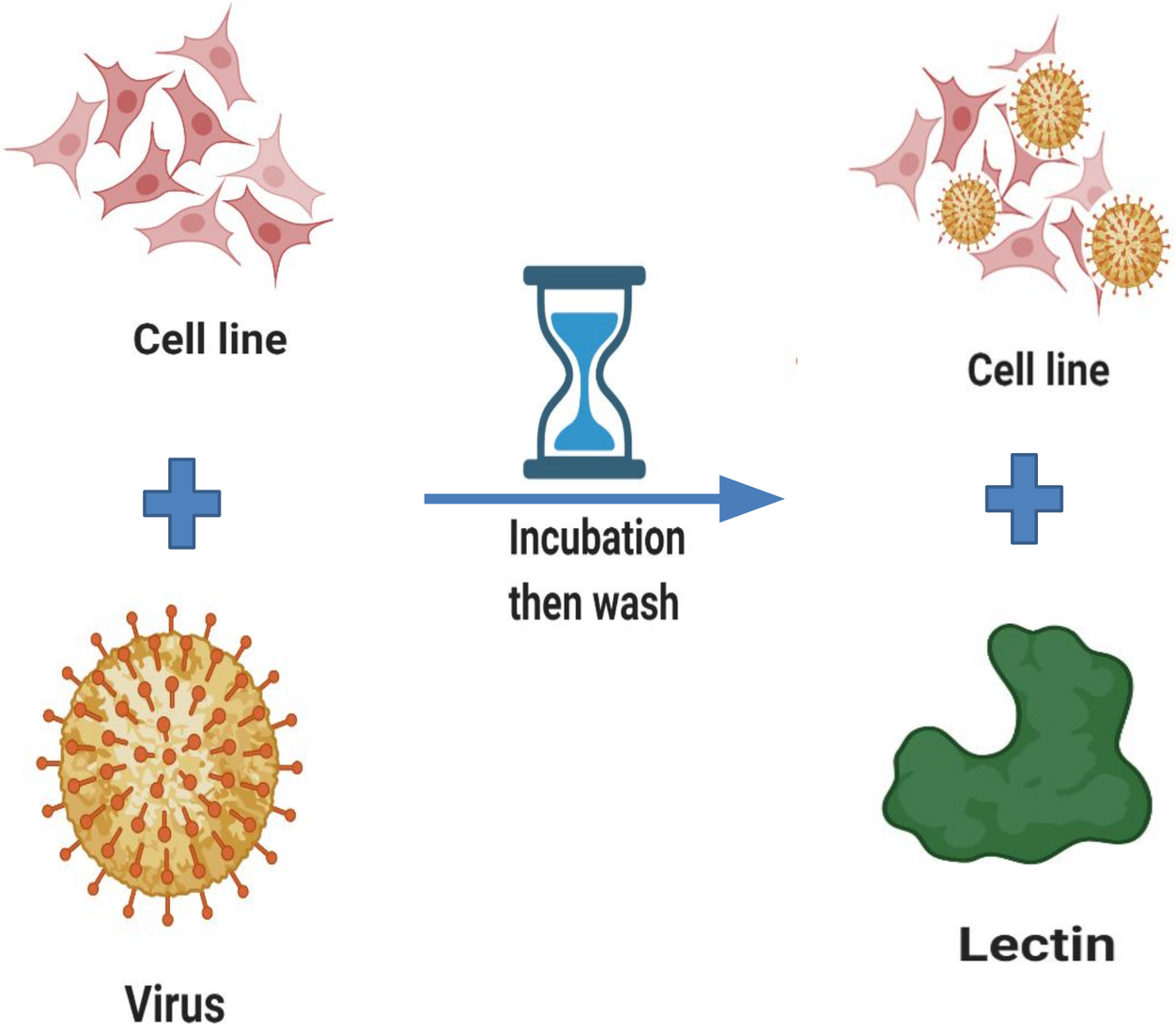


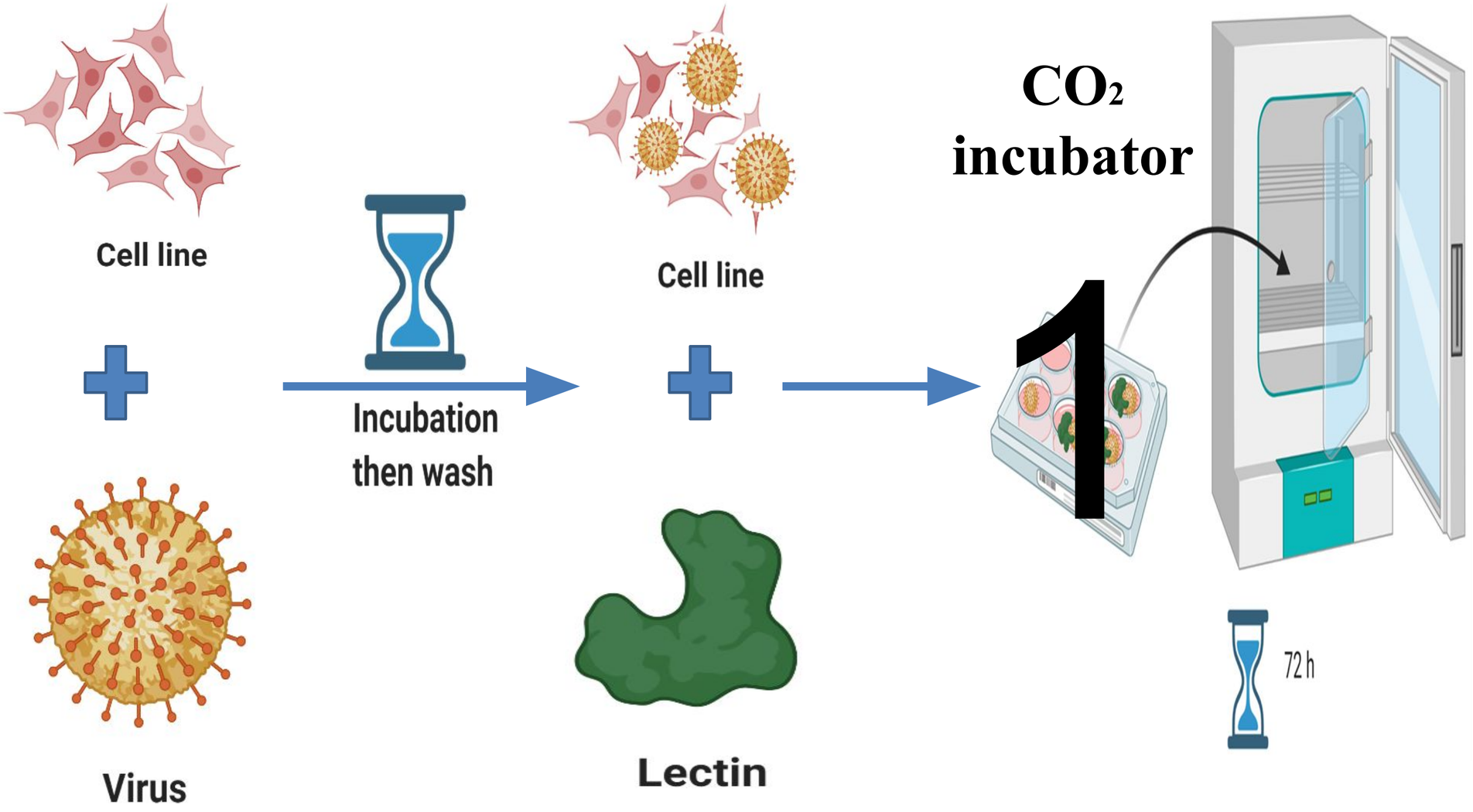
Cell line



Virus

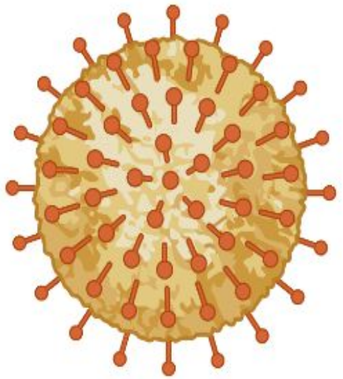
Incubation
then wash


Cell line
Virus
Incubation
then wash
Cell line
Lectin


Cell line
Virus
Incubation
then wash
Cell line
Lectin
CO2
incubator
1
72 h

Lectin

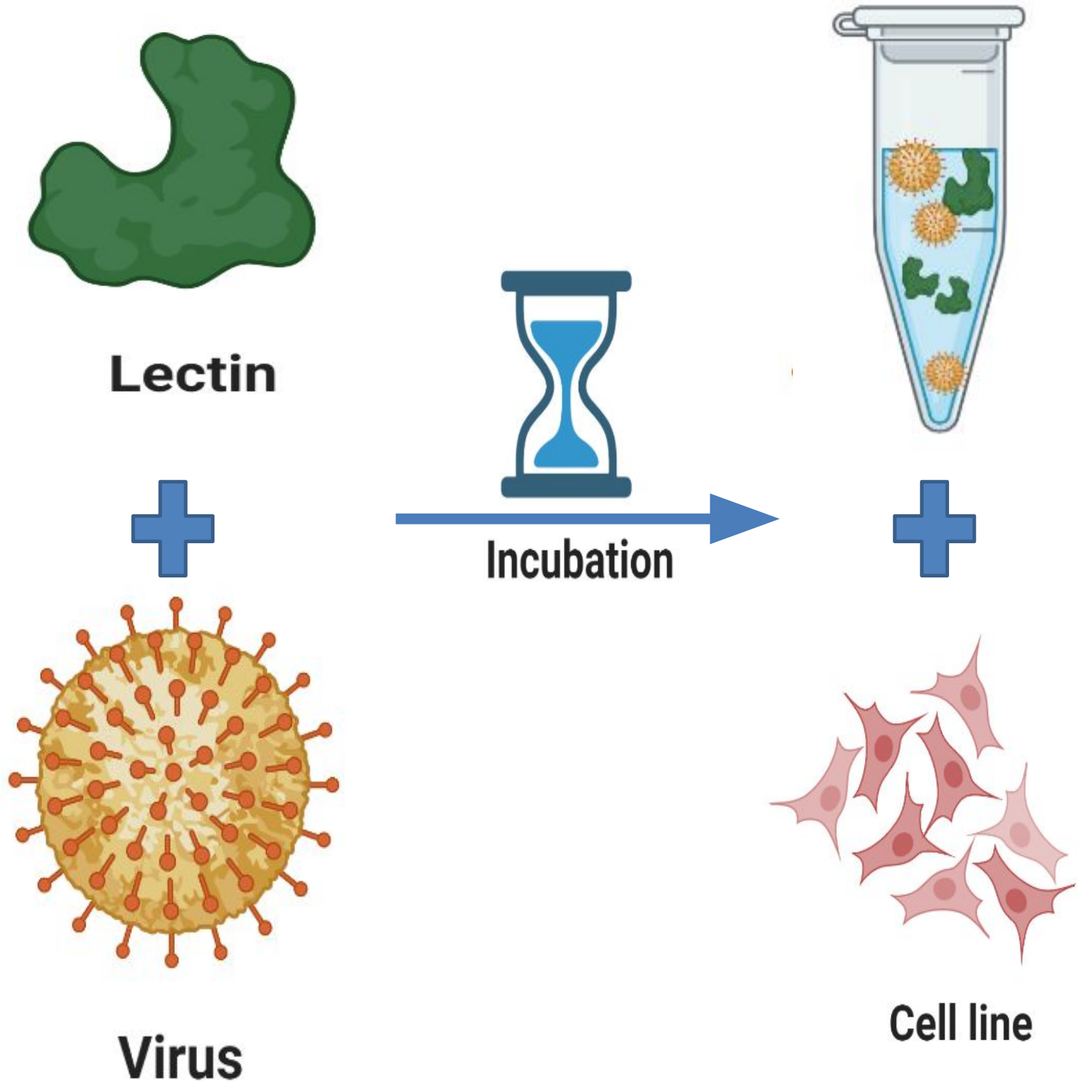
POL

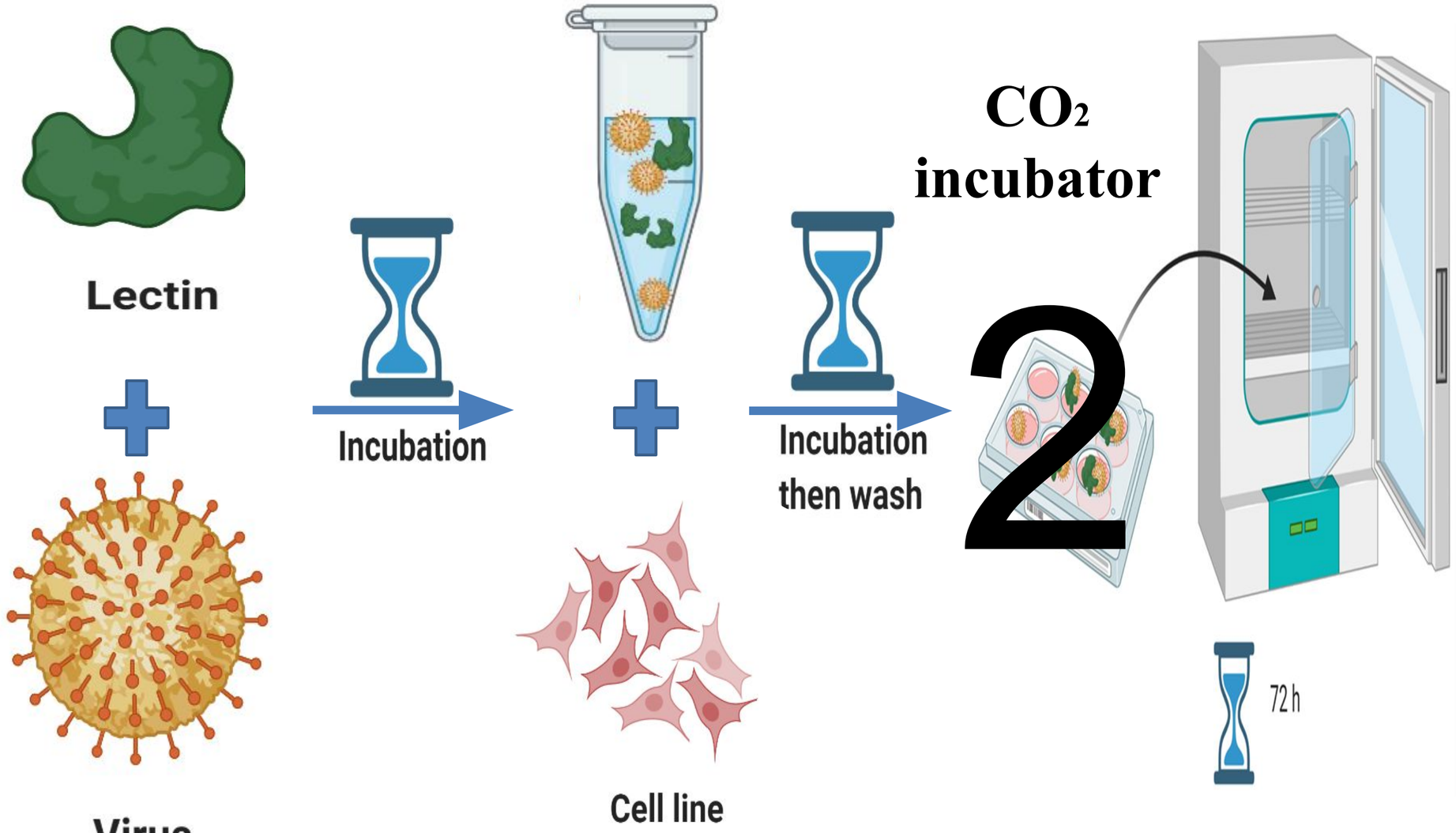


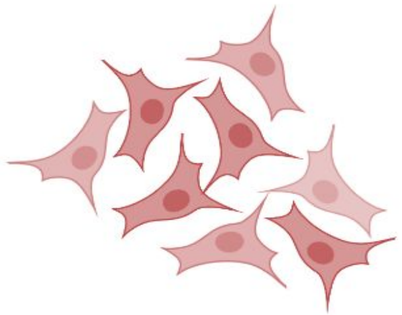
Virus

HBV

Neutralization


Lectin
Incubation
Virus
Cell line


Lectin
Virus
Incubation
Cell line
Incubation
then wash
CO_2
incubator
2
72 h



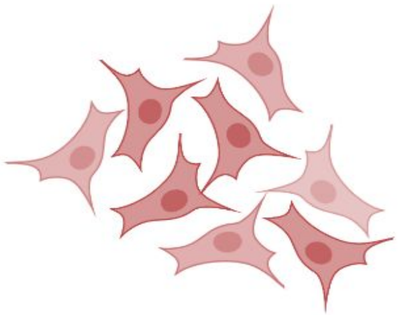
Cell line

HepG2

Blocking

Lectin

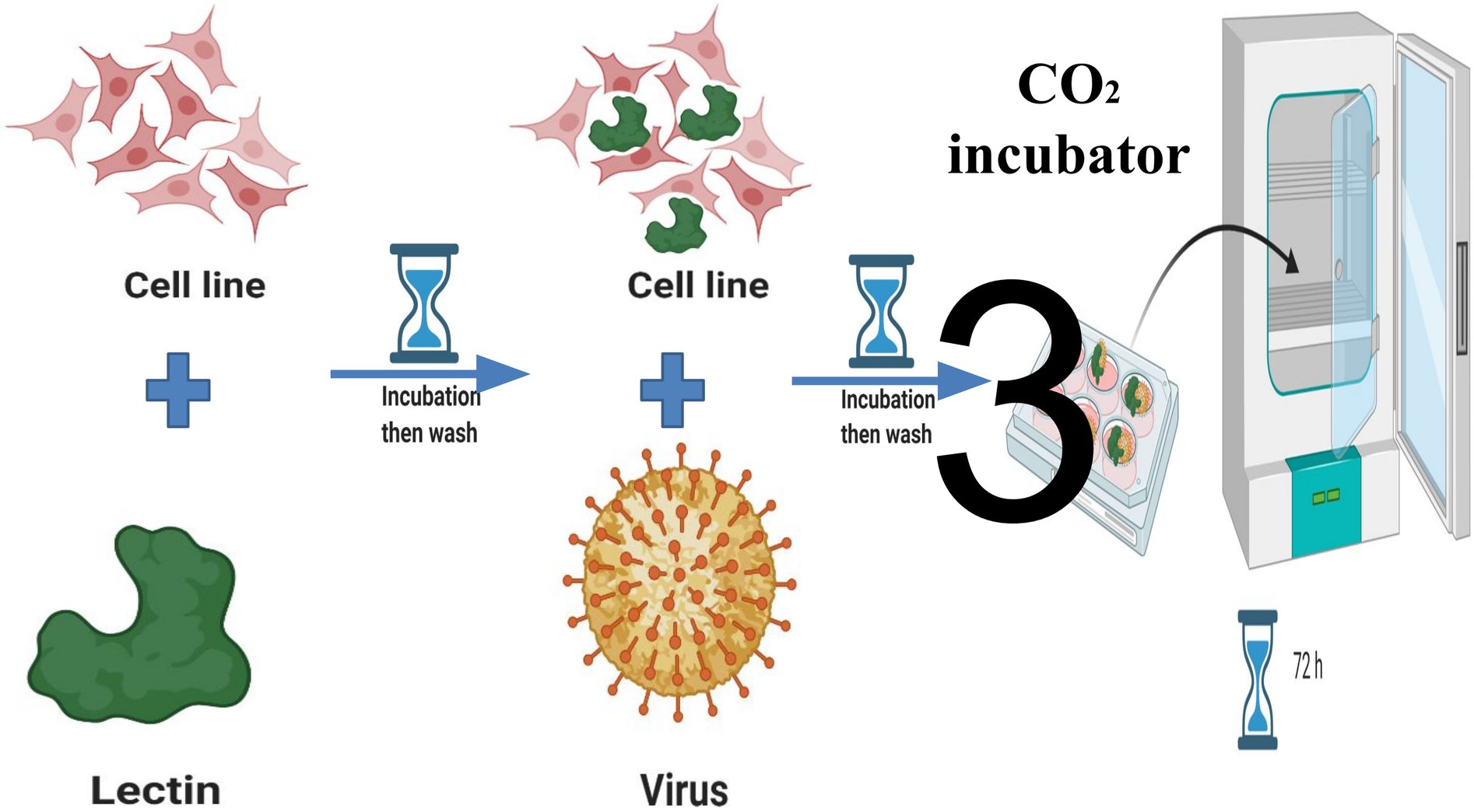
POL



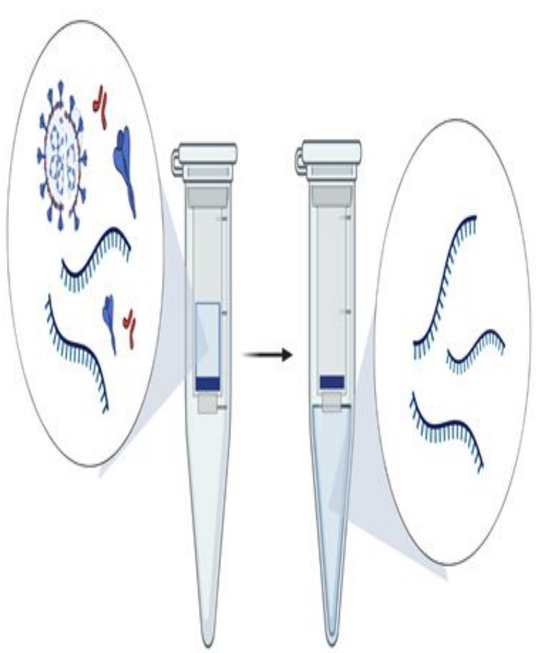
Cell line

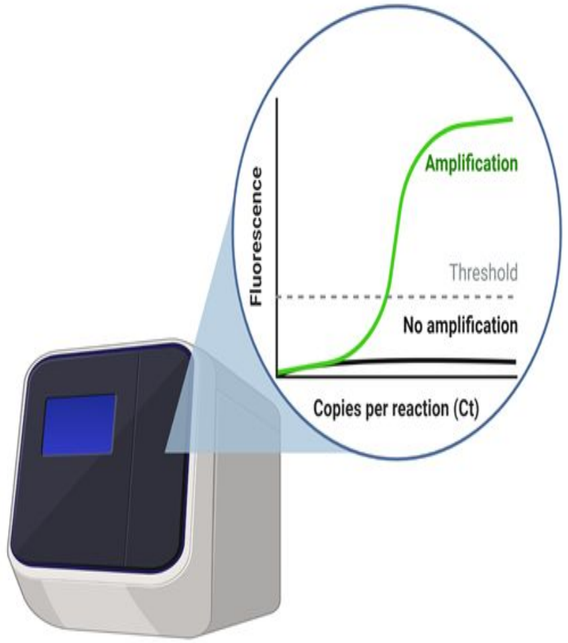
Incubation
then wash

Lectin


Cell line
Lectin
Incubation
then wash
Cell line
Virus
Incubation
then wash
3
CO_2
incubator
72 h

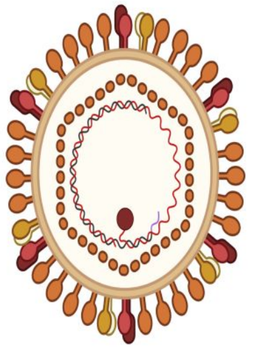
Viral quantification



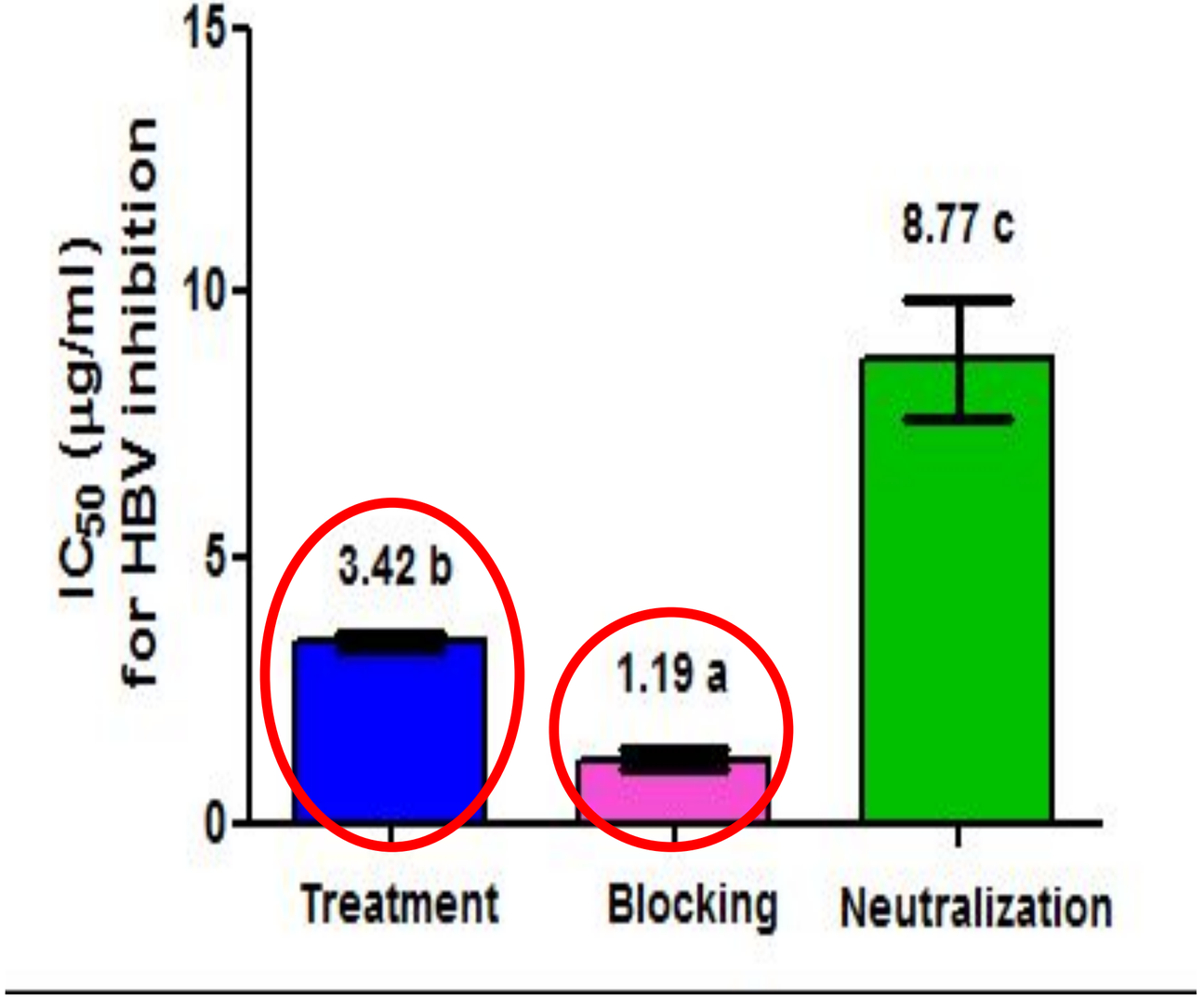


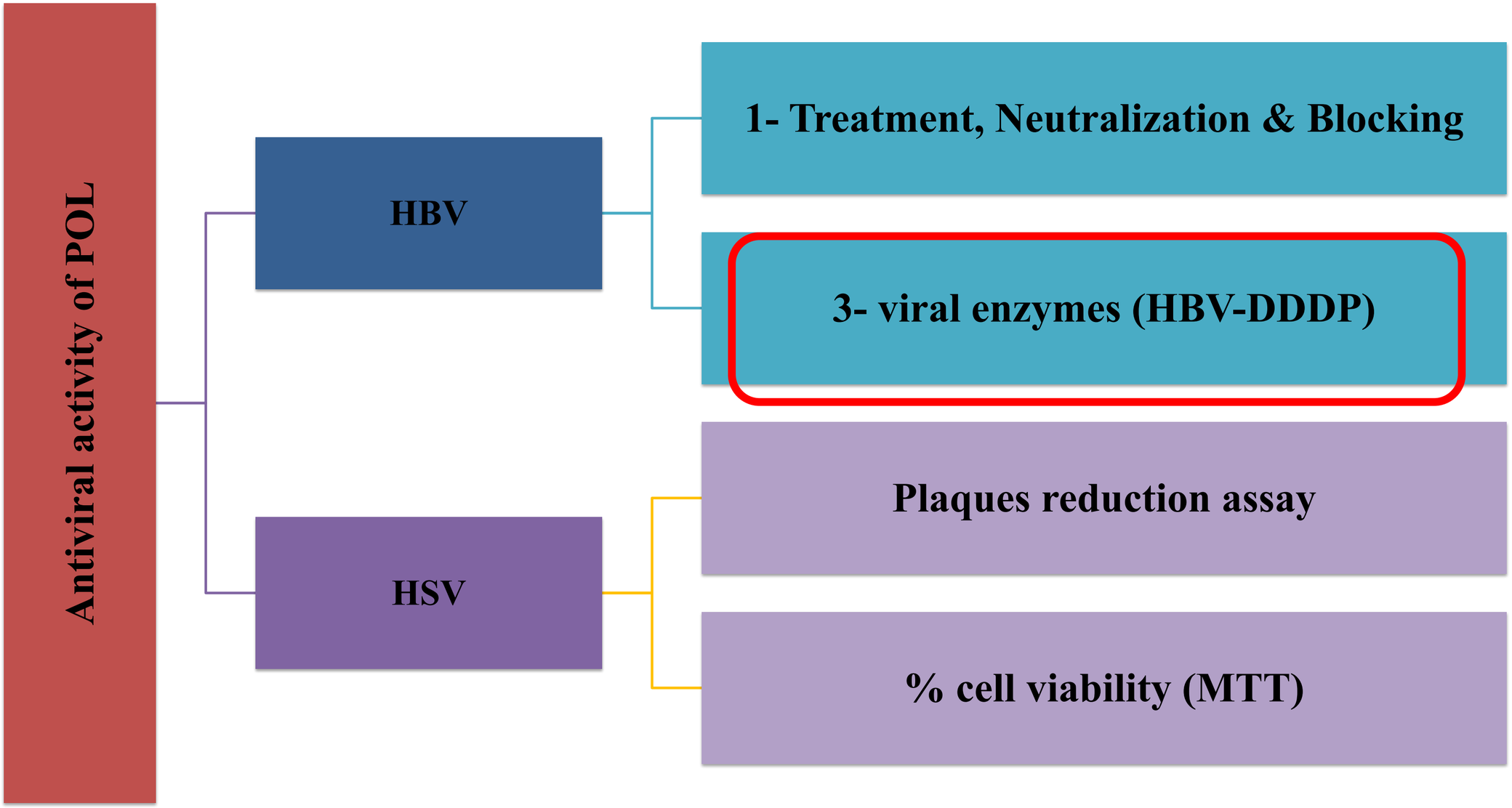
DNA extraction

q-PCR

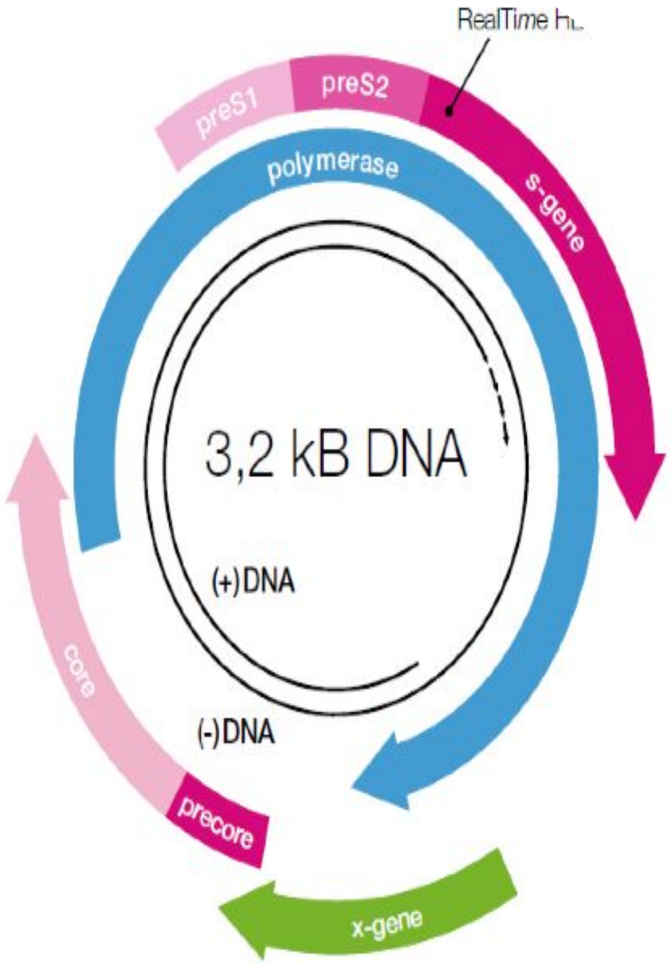


The antiviral activity of POL against HBV




Antiviral activity of POL
HBV
HSV
1- Treatment, Neutralization & Blocking
3- viral enzymes (HBV-DDDP)
Plaques reduction assay
% cell viability (MTT)

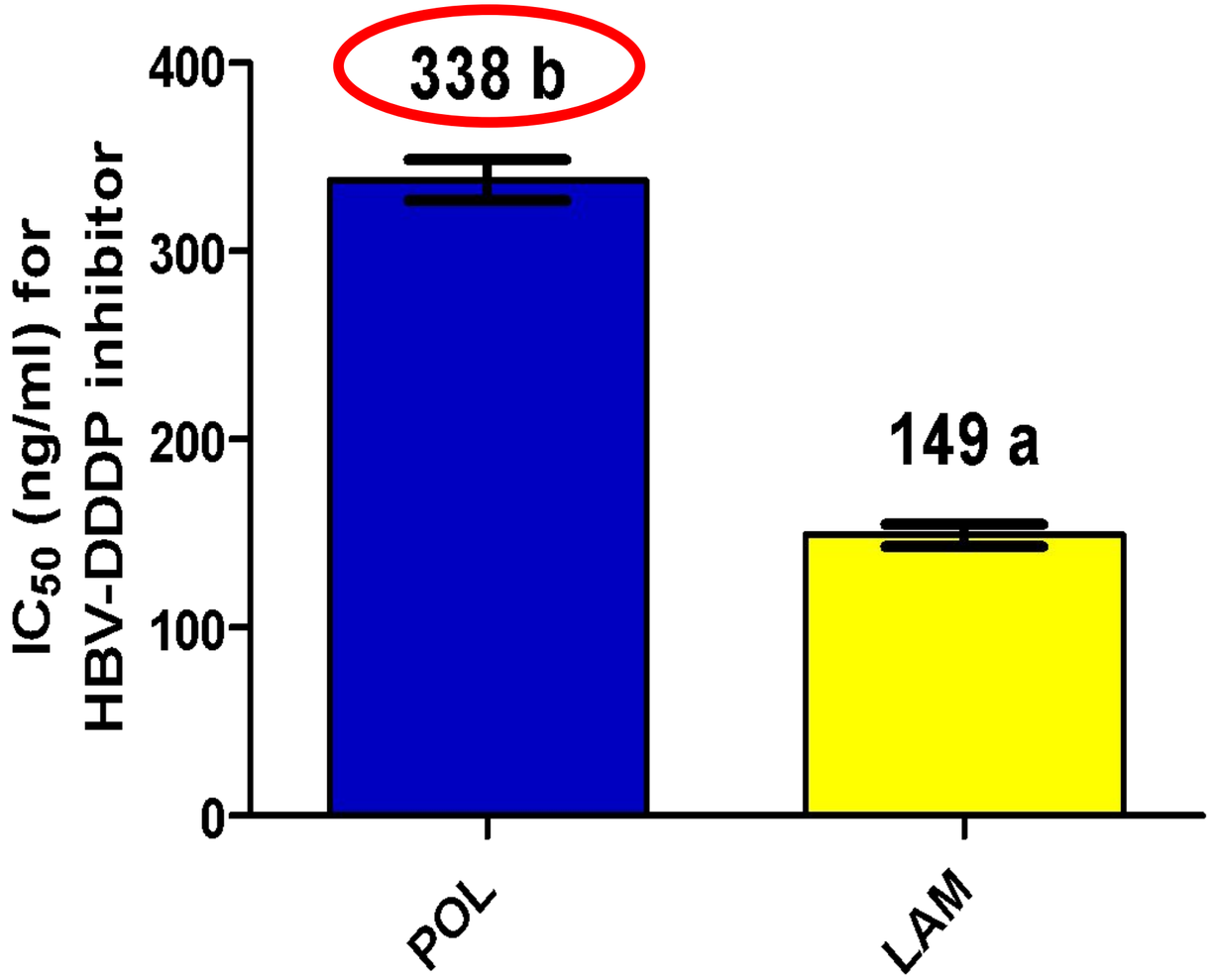
Effect of lectin on HBV DNA-dependent DNA polymerase (DDDP) activity

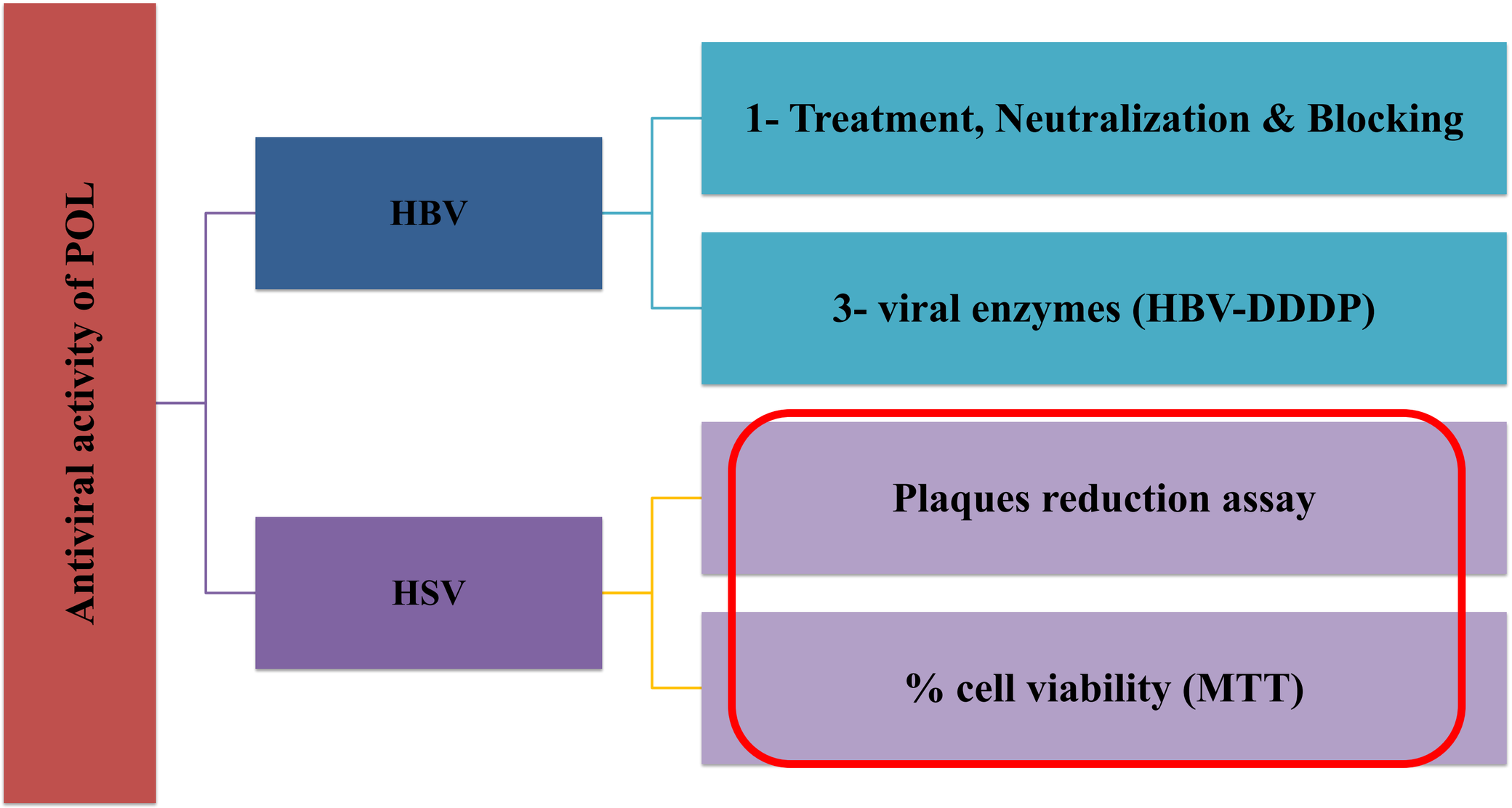


- The inhibitory capacity of lectin on HBV-DDDP was achieved in enzymatic reaction contained a mixture of virus suspension, lectin and radioactive nucleotide (3H-thymidine).
- Then the recovered radioactivity were quantified using scintillation counter.

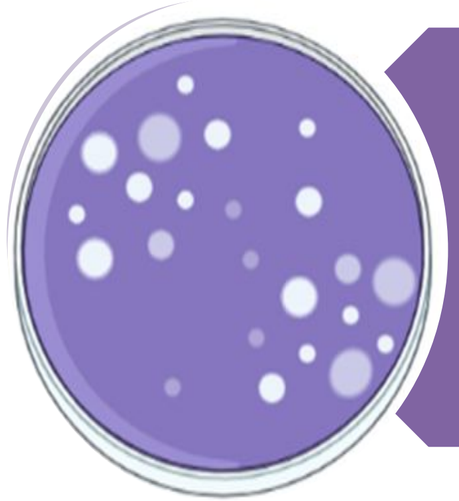
Hirschman, M. Gerber, E. Garfinkel. Differential activation of hepatitis B DNA polymerase by detergent and salt. J Med Virol. 1978;2:61–76.

Effect of lectin on HBV DNA-dependent DNA polymerase (DDDP) activity

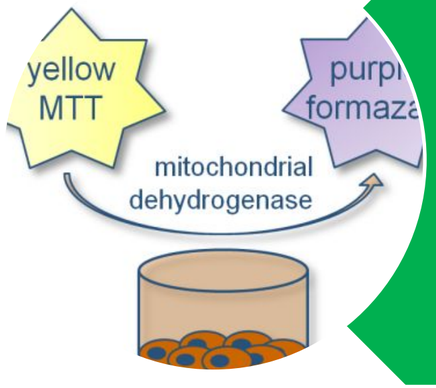



Antiviral activity of POL
HBV
HSV
1- Treatment, Neutralization & Blocking
3- viral enzymes (HBV-DDDP)
Plaques reduction assay
% cell viability (MTT)

IV) *In vitro* detection of antiviral activity of POL against HSV

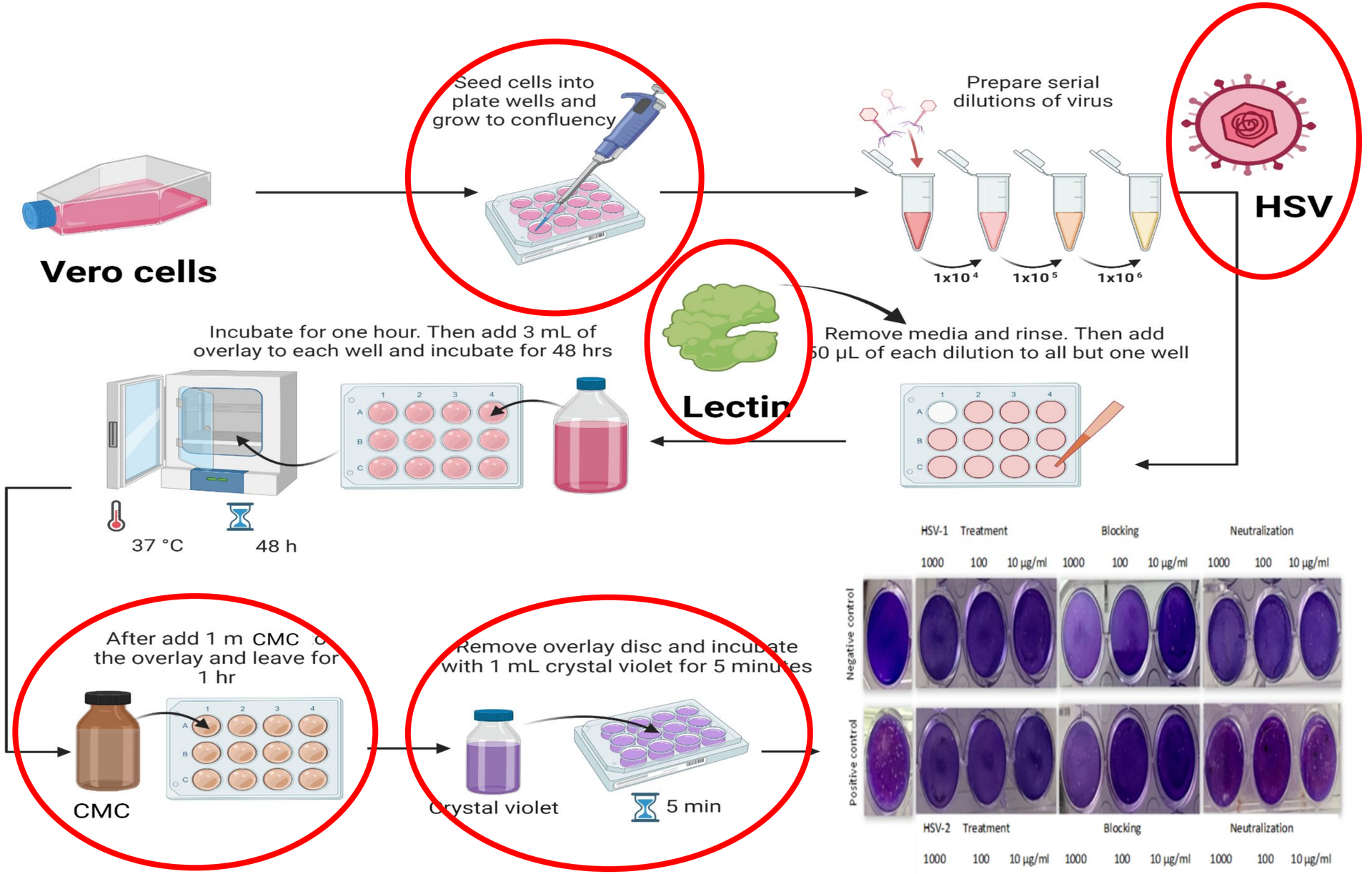


1) Plaques reduction assay

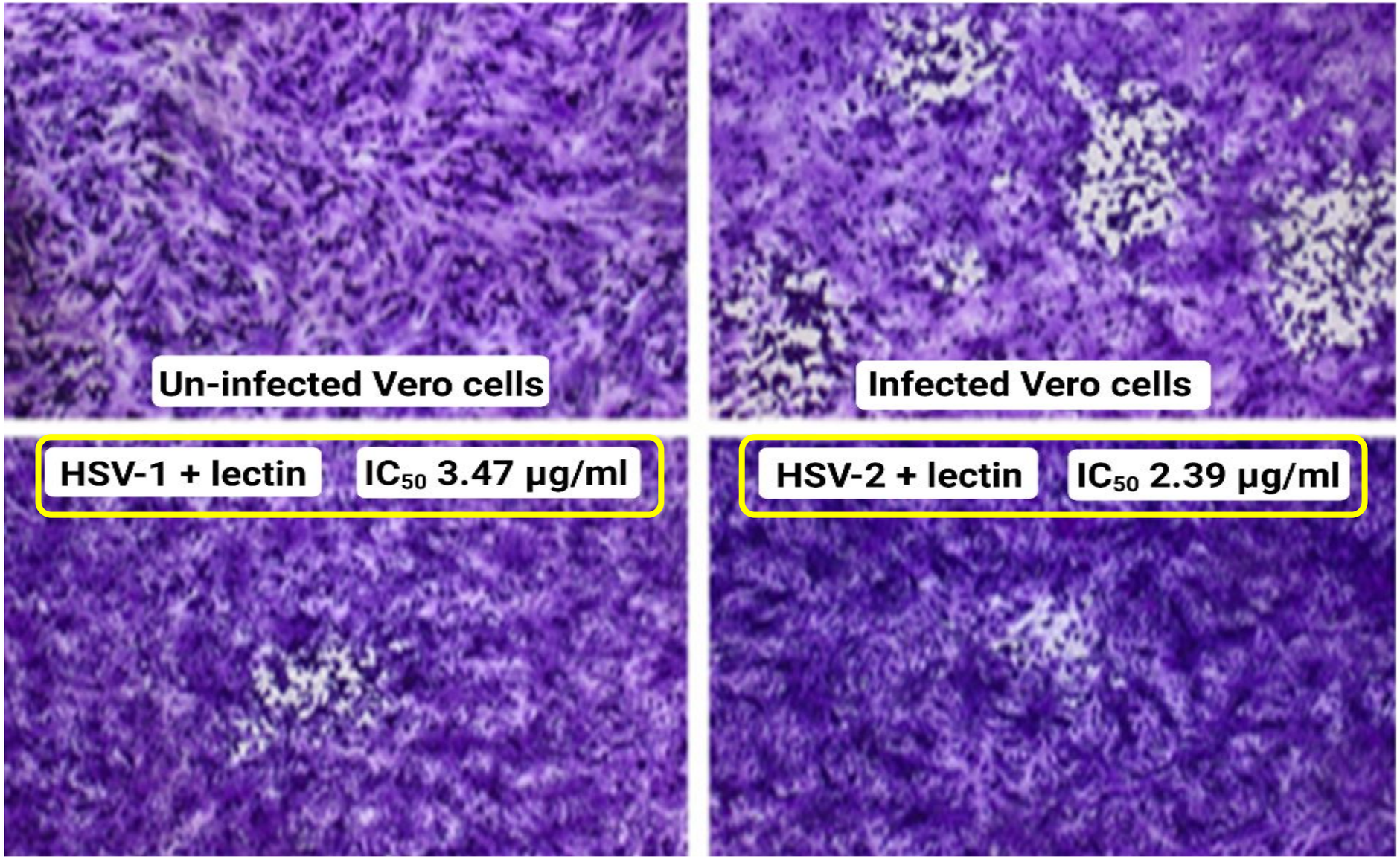


2) Cell viability (MTT)

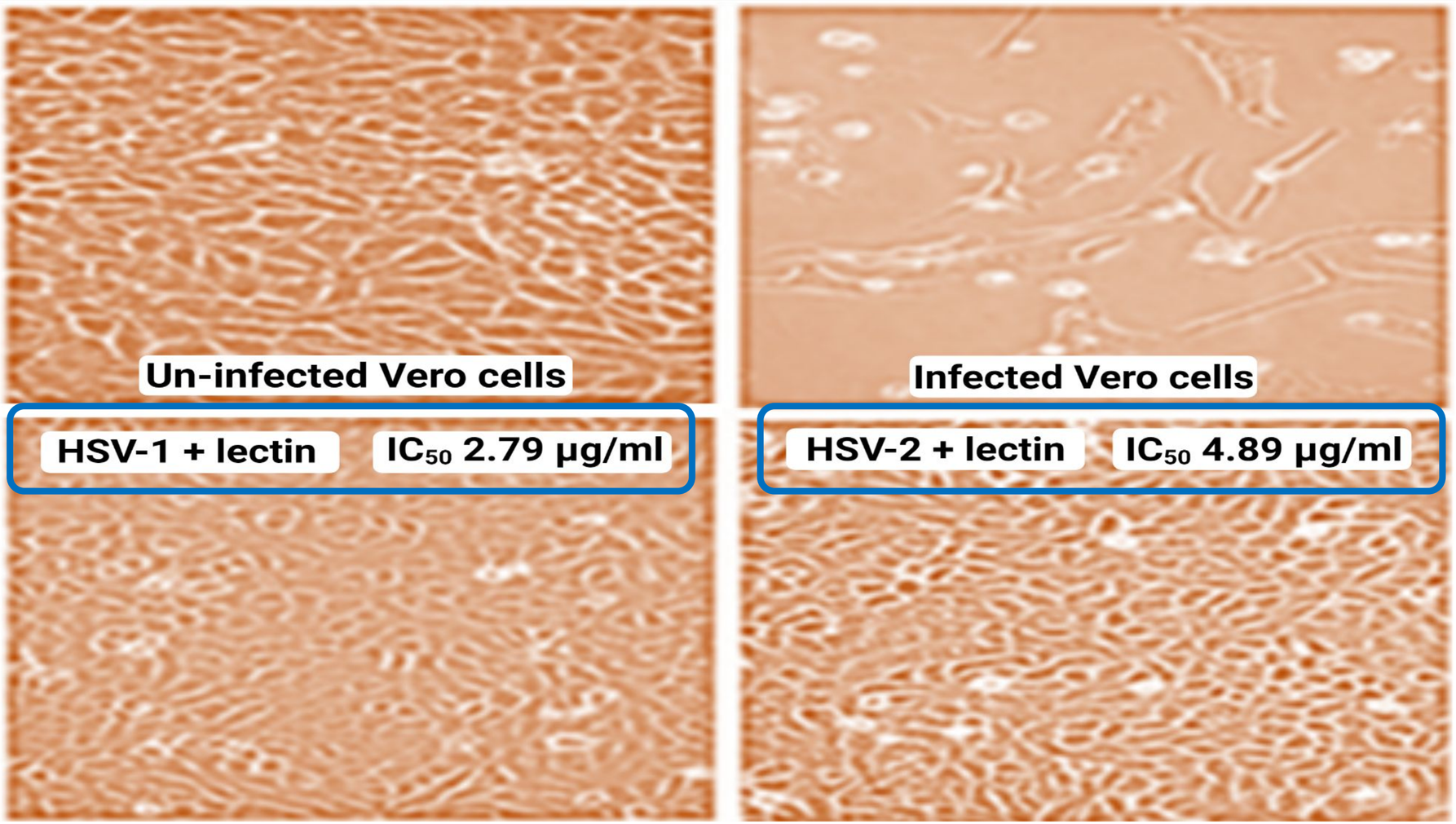
1) Plaques reduction assay



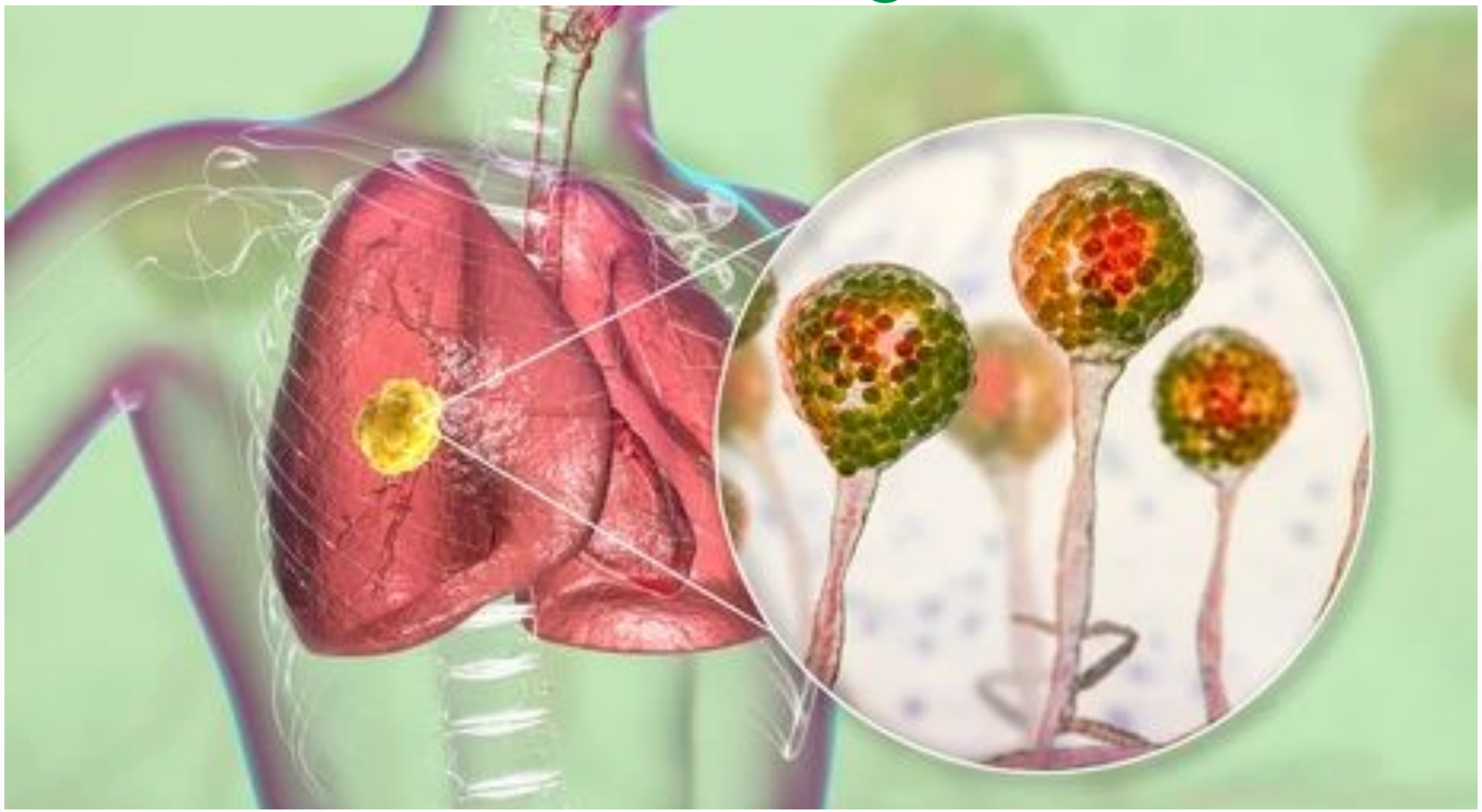
1) Plaques reduction assay



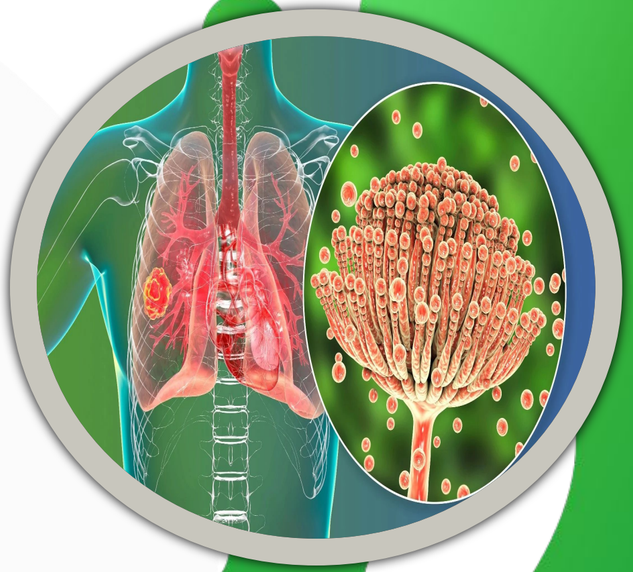
2) Cell viability % (MTT)



Risks and Threats of Fungi



COVID-19 associated pulmonary aspergillosis (CAPA)



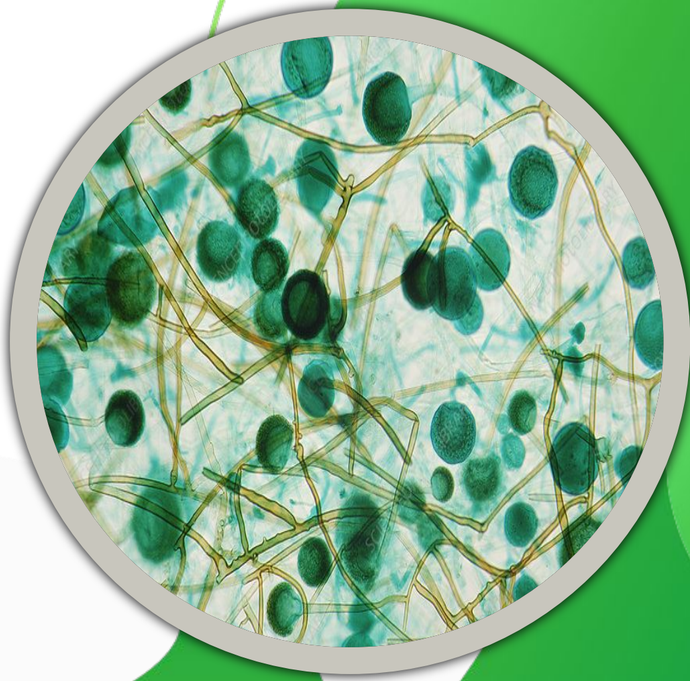
COVID-19 associated pulmonary aspergillosis (CAPA) were reported from China in early 20201. Since then, multiple case series and cohort studies have highlighted the importance of this potentially life-threatening secondary infection, sometimes caused by azole-resistant Aspergillus spp. Predominant such as *A. fumigatus*.

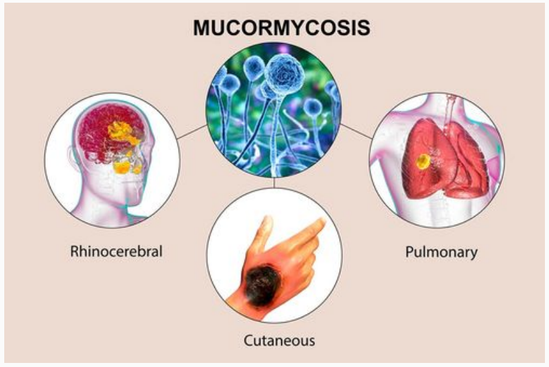
02

03

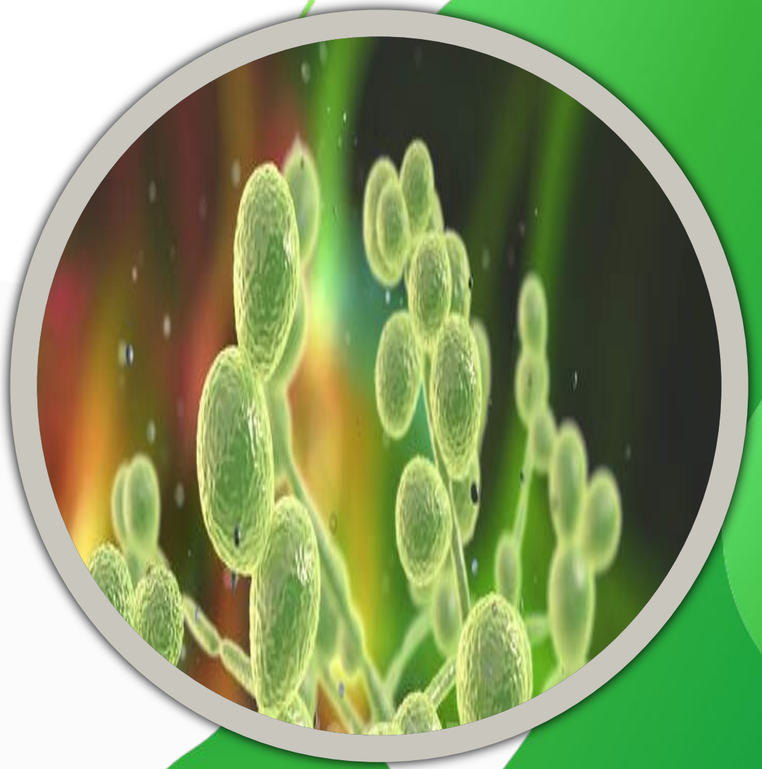
COVID-19 associated mucormycosis (CAM)

COVID-19 associated mucormycosis (CAM) gained worldwide attention in early 2021, during the second wave of the COVID19 pandemic in India. An unprecedented surge of cases of mucormycosis, a fungal infection caused by moulds belonging to the order Mucorales, posed a major healthcare problem with > 47,500 cases reported by the Indian government between May and August 2021. Where *Rhizopus* spp. are predominant.



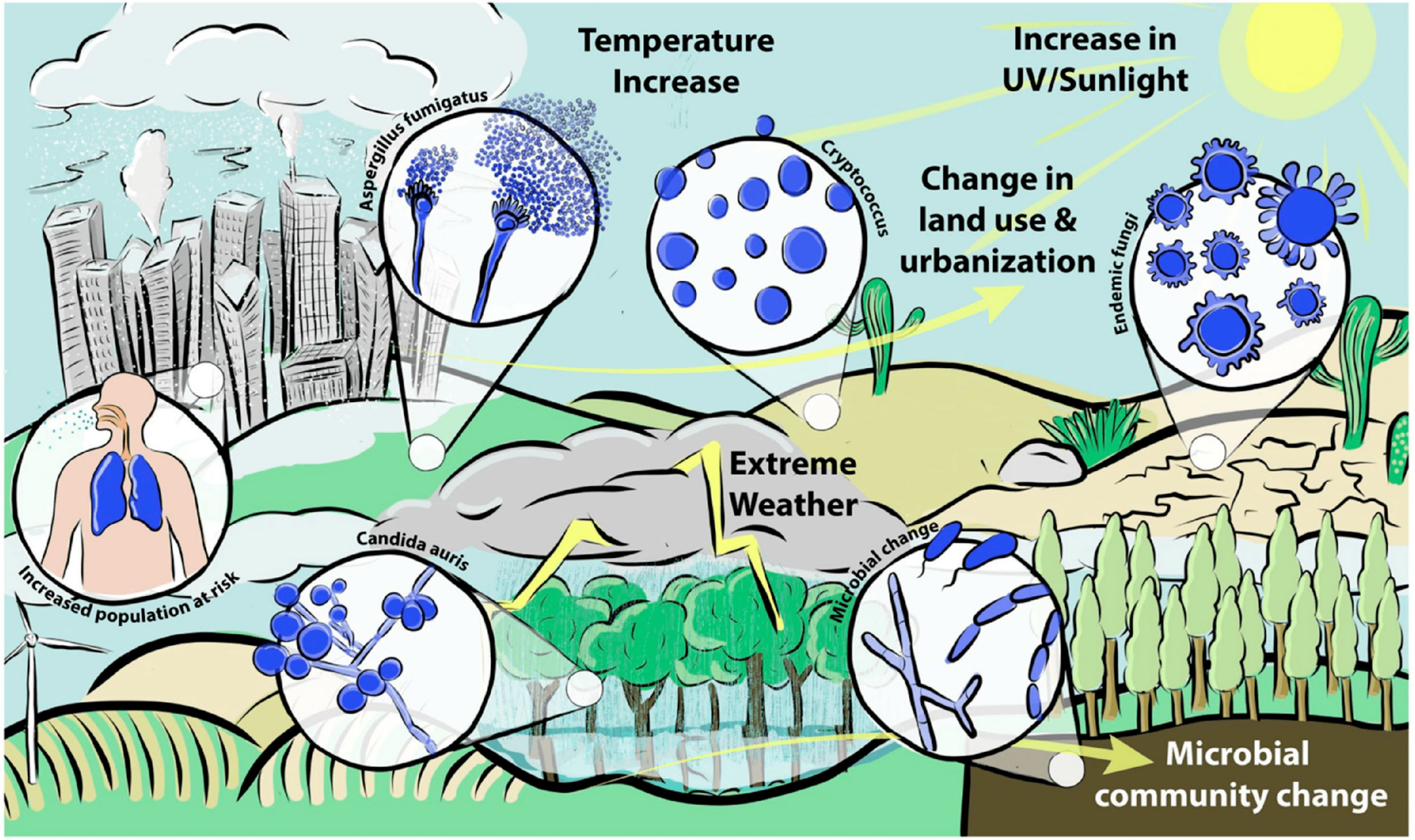


Invasive Candida infections



Invasive Candida infections in patients with COVID-19 in the intensive care unit (ICU) were first described shortly after the emergence of SARS-CoV-2. Where *C. albicans* are predominant specially *C. auris*

Climate Change Exacerbating Fungal Disease Disparities



Climate Change Exacerbating Fungal Disease Disparities

The increase in global temperature has caused disparities in mycoses: the appearance of new pathogens, such as *Candida auris* and *Trichophyton indotineae*, an increase in the severity of cases of blastomycosis and dermatophytosis, exacerbation of allergies, as well as the appearance of mycoses considered endemic in different non-endemic areas. This situation constitutes a wake-up call to focus efforts on adequately diagnosing and treating these diseases.

References:

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THANK YOU

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