EXPLORATION OF NATURAL RESOURCES OF POTENTIAL CANDIDATES FOR NOVEL THERAPEUTIC AGENTS

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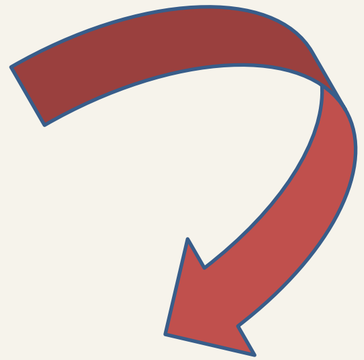
INTRODUCTION

Pharmacotherapy has made rapid progress since the early 20th century.



Synthetic and semi-synthetic chemicals → in modern medicines.

MAIN STAGES AND TRENDS IN THE DEVELOPMENT OF CHEMICAL TREATMENT

Early Period of Chemical Medicine Development (19th - Early 20th Century)

Discovery of Aspirin (1897)

Discovery of Sulfa (1930s)

Antibiotic Revolution (1930s - 1950s)

Discovery of Penicilin (1928)

Development of Other Antibiotic Classes: streptomycin, tetracyclines, cephalosporins

MAIN STAGES AND TRENDS IN THE DEVELOPMENT OF CHEMICAL TREATMENT

The Era of Chemotherapy and Cancer Treatment (1950s - 1970s)

Chemotherapy Development

Hormones and Antihormones

Structure-Based Drug Improvement (1970s - 1990s)

Molecular Target-Based Medicine

Anti-HIV Medicine Development

MAIN STAGES AND TRENDS IN THE DEVELOPMENT OF CHEMIC TREATMENT

The Era of Biotechnology and Antibody-Based Medicine (1990s - Present)

Monoklonal Antibodies (mAbs)

Biological Medicine

Personalized Medicine (2000s - Present)

Pharmacogenomics

Specific Target Inhibitors

MAIN STAGES AND TRENDS IN THE DEVELOPMENT OF CHEMIC TREATMENT

Small Molecule and RNA Therapeutics Development (2010s - Present)

RNA and mRNA therapy

Small Molecule Inhibitors

Regenerative Medication and Gene Therapy (Present and Future)

Gene Therapy

Stem Cell Therapy

CHALLENGE

Despite many advances in chemical treatment, challenges such as antibiotic resistance, medicine side effects, and the cost of developing new medicines continue to be problems.

- Side effects
- Allergic Reaction
- Drug Resistance
- Toxicity
- Drug Interactions
- Addictions and misapplication
- Effects on the Immune System
- Treatment Failure
- Genetic Mutation
- Risks to Pregnancy and Fetus

PROBLEMS

Natural ingredients, or substances derived from nature such as plants, animals, and minerals, have been used in therapeutic treatments for thousands of years.

Currently, the potential of natural materials is often neglected compared to chemical materials.

Nowadays, the benefits of natural substances continue to be explored in modern medicine.

ADVANTAGES AND DISADVANTAGES OF PHARMACOTHERAPY

ADVANTAGES	DISADVANTAGES
Effective and measurable	more obvious side effects
Consistent dosage	Drug dependency
Under the supervision of a doctor, so that monitoring side effects is easier.	the body may become resistant or require higher doses over time

ADVANTAGES AND DISADVANTAGES OF PHYTOPHARMACOLOGIES

ADVANTAGES	DISADVANTAGES
Lighter on the body	Lack of dosage standards
Less risk of side effects	Natural ingredients can interact with chemical medicine and affect their effectiveness or pose risks.
Natural remedies are often used in a holistic approach that considers the overall balance of the body.	Some natural ingredients may not be as effective as chemical medicine, especially for serious medical conditions.

The use of natural ingredients for disease prevention has long been part of health traditions in many cultures.

Some natural ingredients have antioxidant, anti-inflammatory and immune system supporting properties that can help prevent disease.

These natural ingredients can be included in the daily diet to help maintain health and prevent disease.

SOME NATURAL INGREDIENTS AS PHYTOPHARMACOLOGIES

- Turmeric(Curcuma longa)
- Ginger (Zingiber officinale)
- Sambiloto (Andrographis paniculata)
- Curcuma (Curcuma xanthorrhiza)
- Honey
- Aloe Vera
- Soursop leaf(Annona muricata)
- Ginseng (Panax ginseng)
- Cinnamon(Cinnamomum verum)
- Bay leaf(Syzygium polyanthum)
- Rosella (Hibiscus sabdariffa)
- Red Sappanwood (Caesalpinia sappan L)

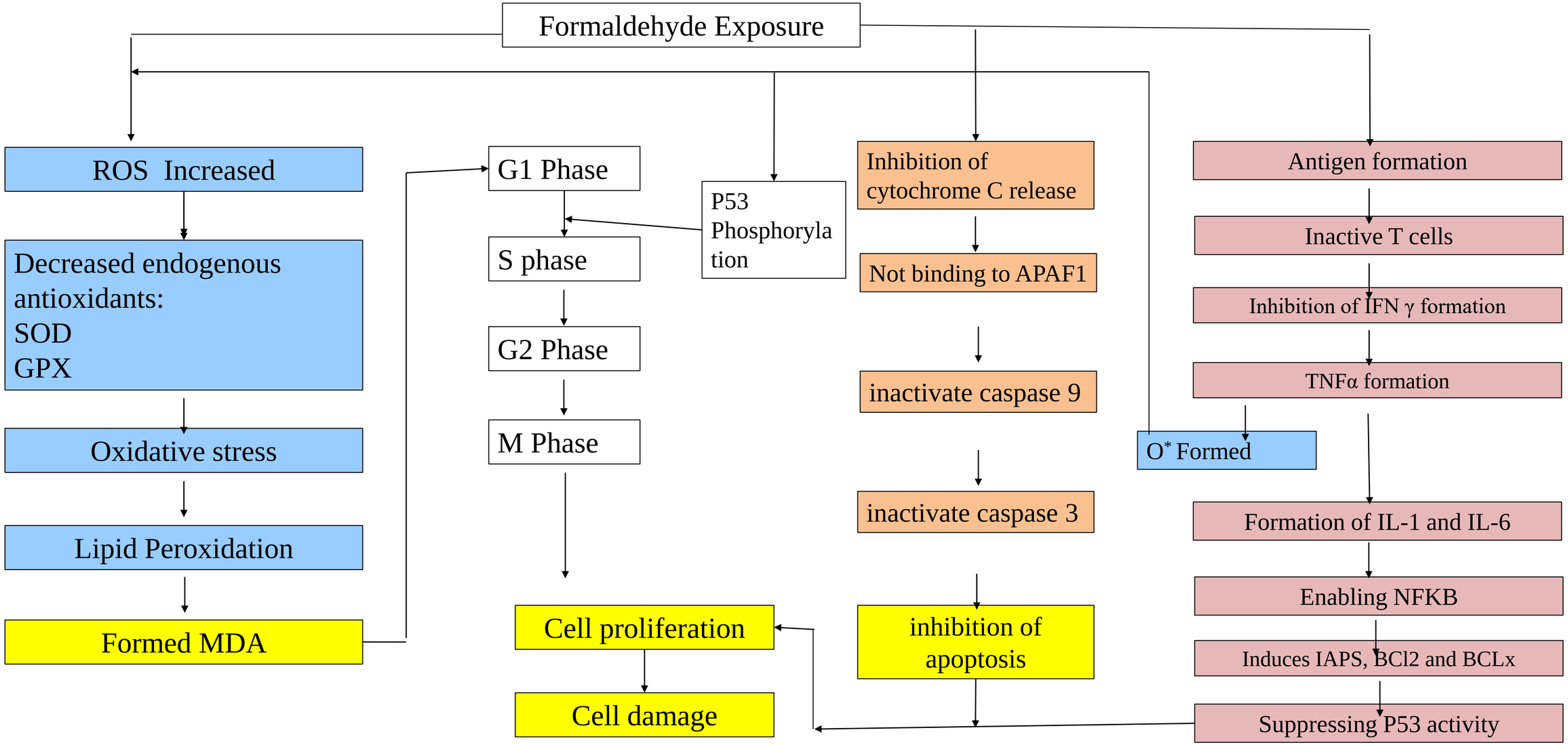
MAIN BENEFITS OF NATURAL INGREDIENTS IN TREATMENT THERAPY

- Source of Active Substances
- Antioxidant Effects
- Anti-inflammatory
- Antimicrobial and Antivirus
- Adaptogen
- Immunomodulator
- Neuroprotective
- Good for Digestive health
- Reduction of Side Effects
- Complementary Modern Therapy

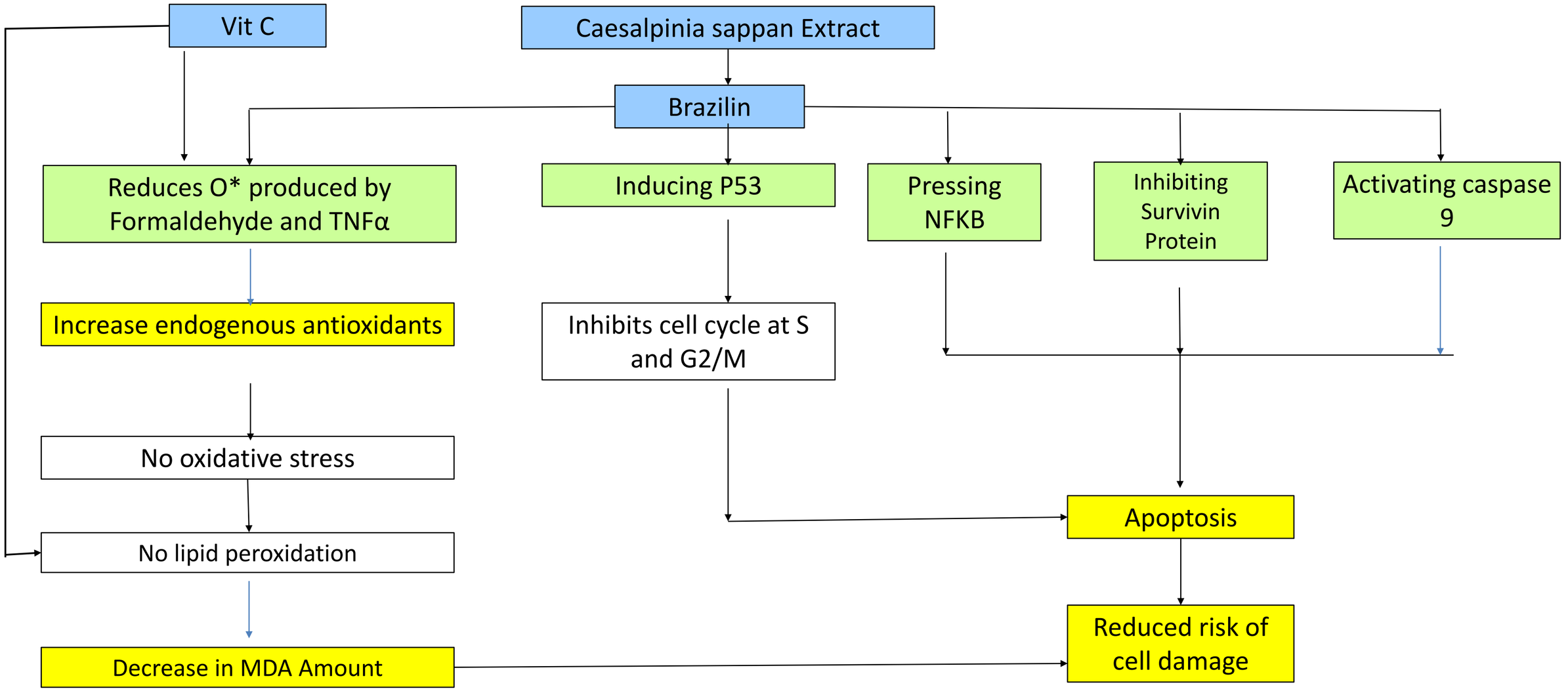
BENEFITS OF SAPPANWOOD EXTRACT IN PREVENTING OXIDATIVE STRESS, LIPID PEROXIDATION AND CELL DAMAGE

Study on SOD, MDA, Caspase 3 Levels, and Nasal Epithelial Damage in *Sprague Dawley* Rats Exposed to Formaldehyde Gas

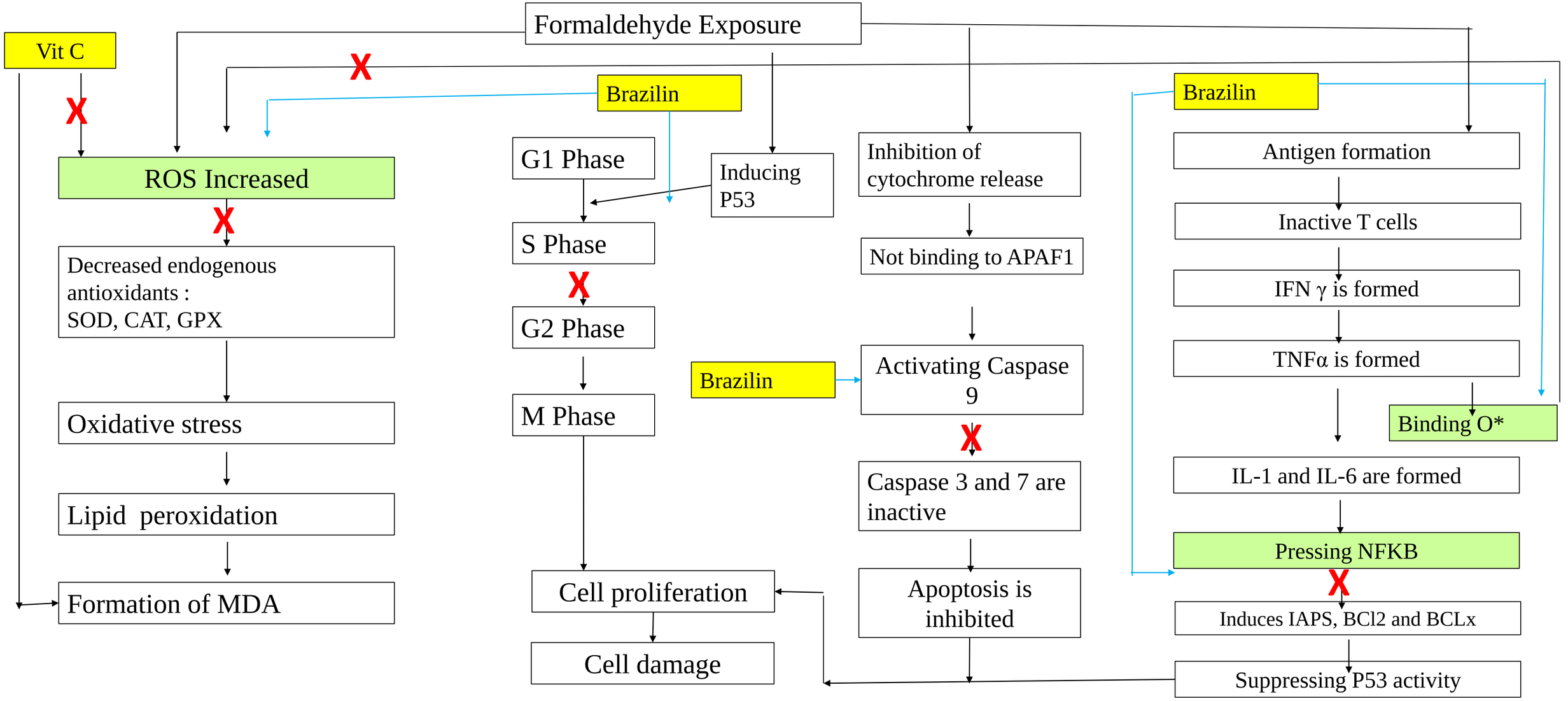
Mechanism of Cell Proliferation by Formaldehyde



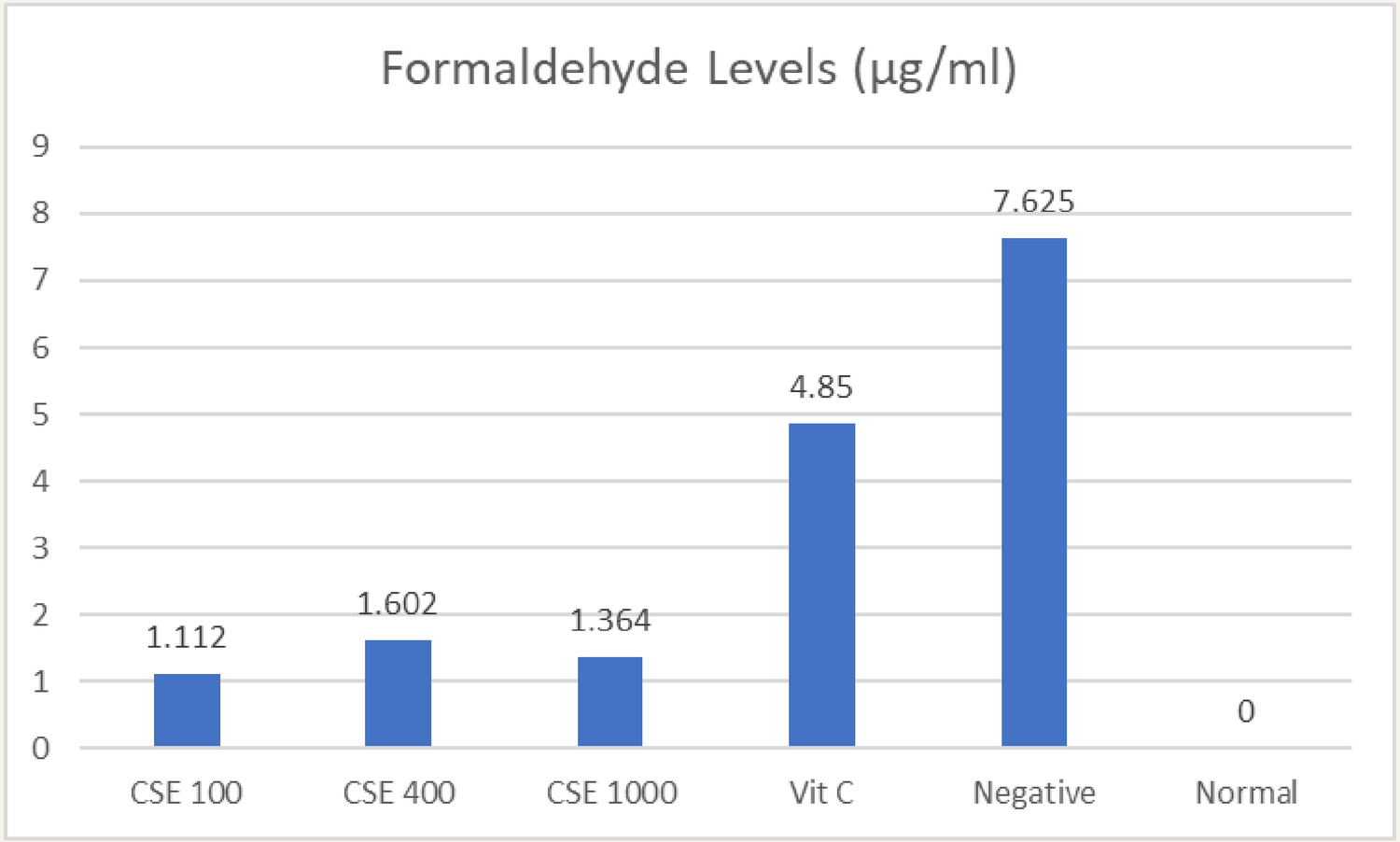
Mechanism of Action of Secang Wood Extract and Vitamin C in Preventing Fat Peroxidation and Cell Proliferation



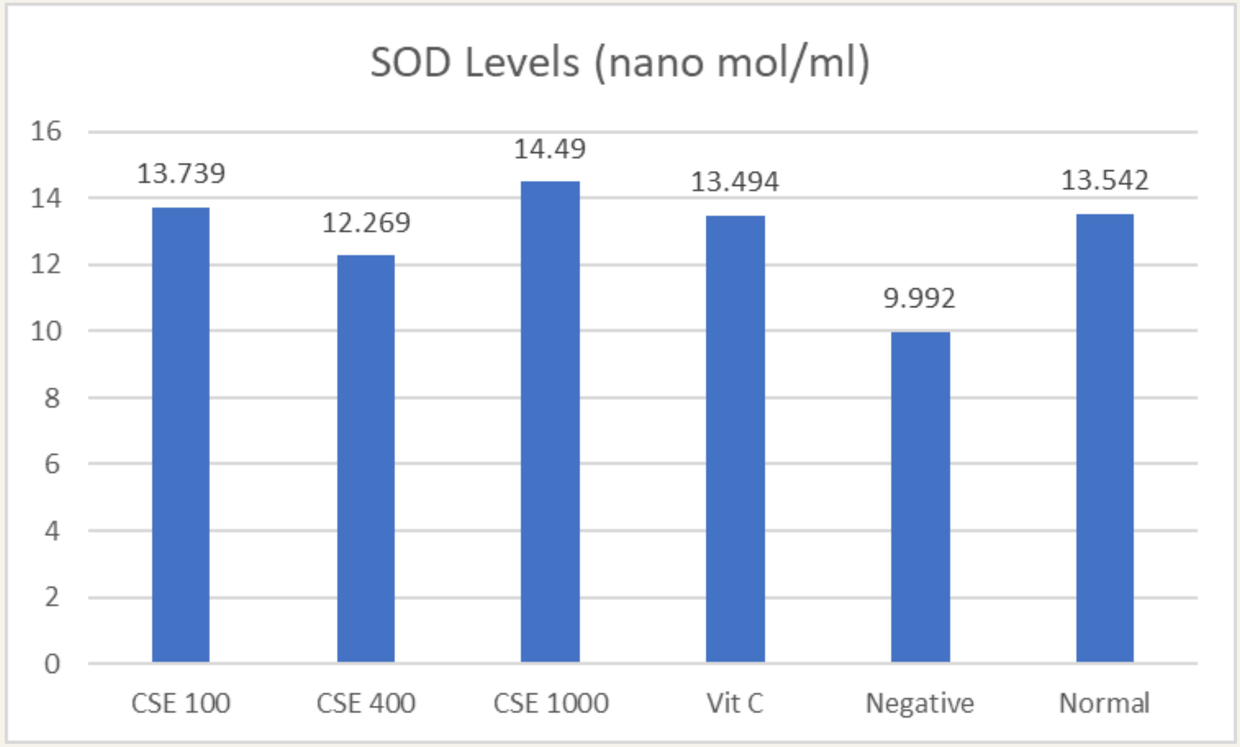
Inhibition Point of Cell Proliferation By Brazilin and Vit C

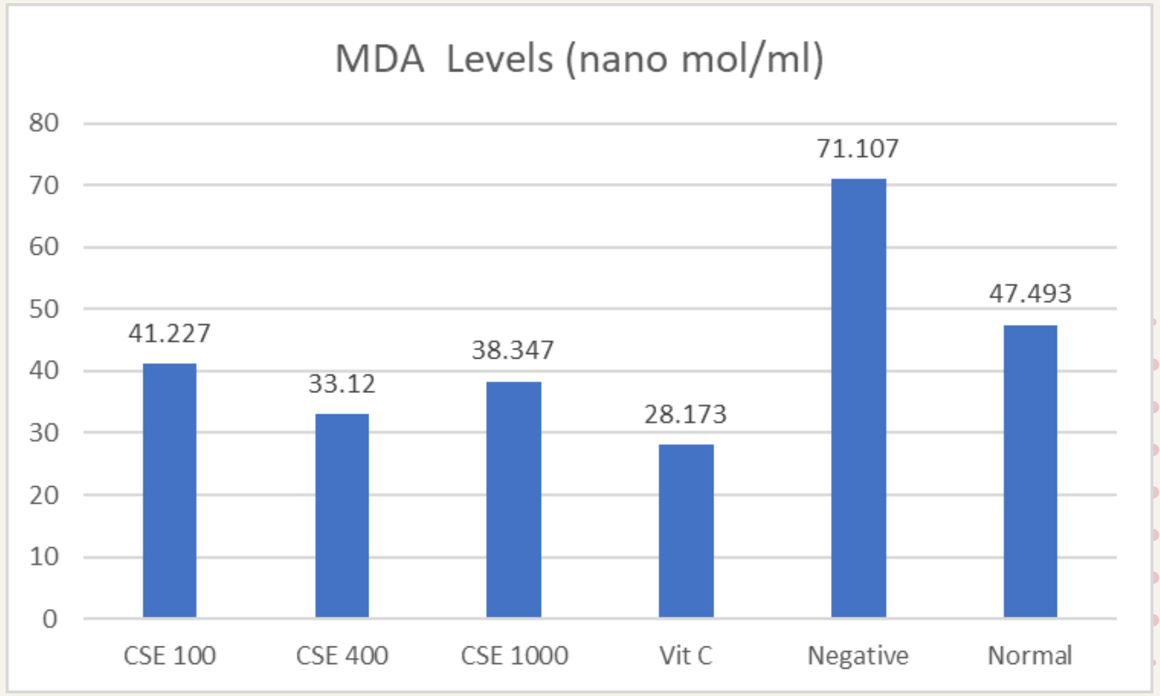


Formaldehyde Levels

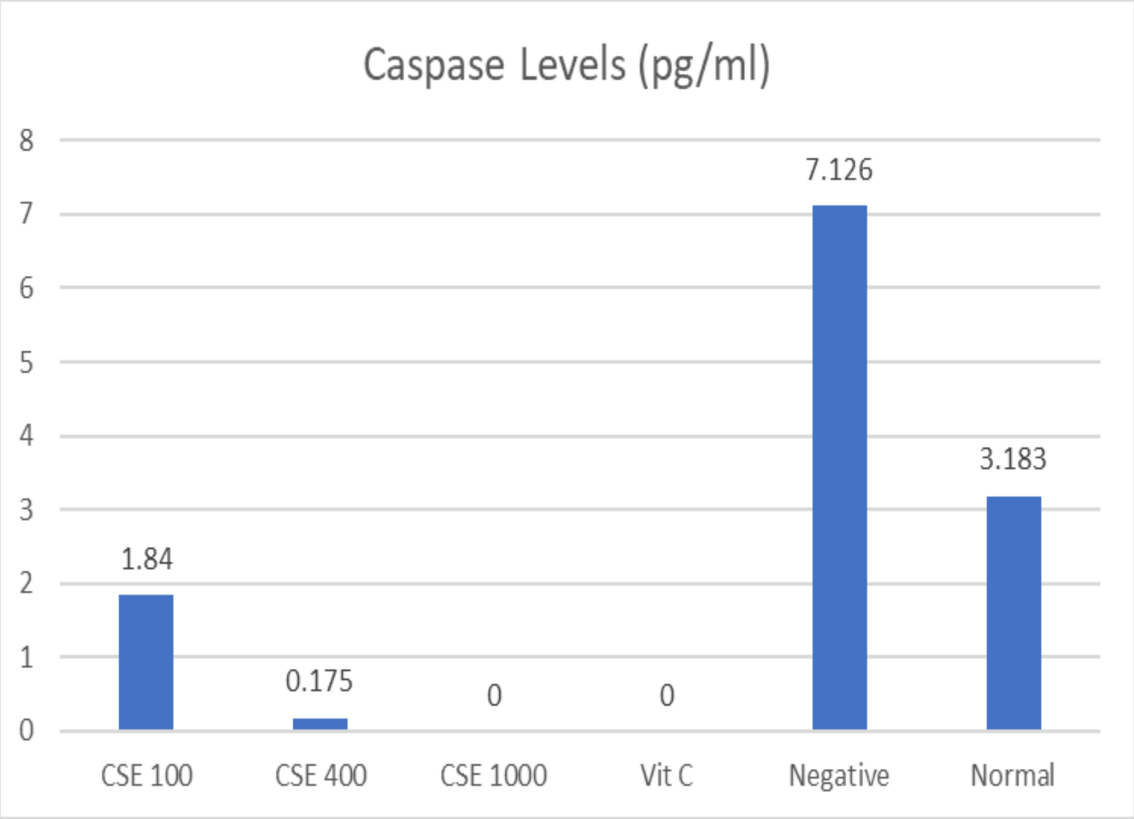


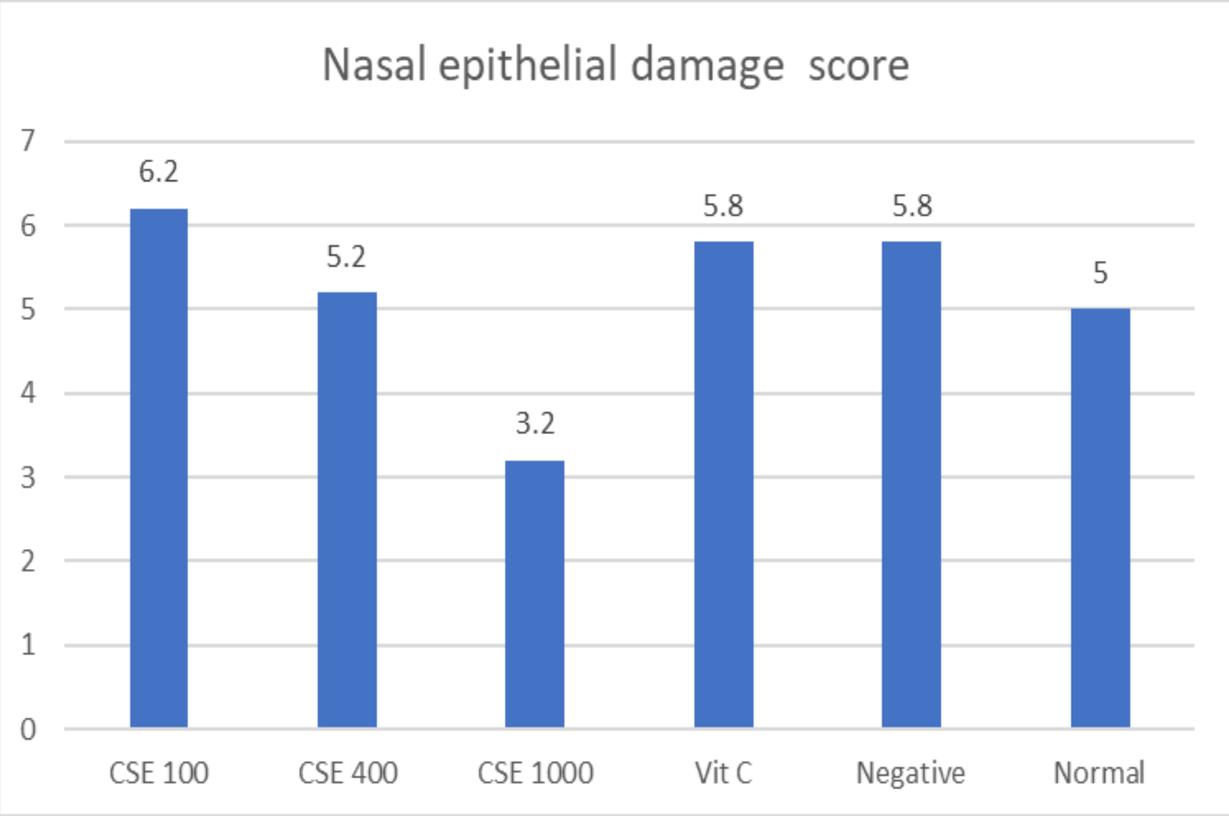
SOD and MDA Levels

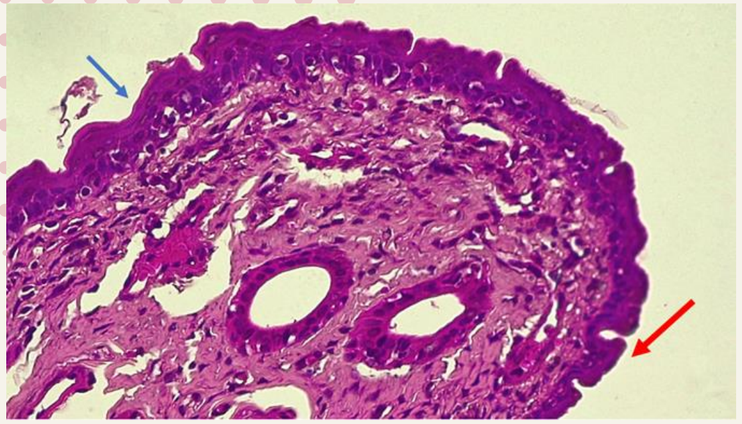




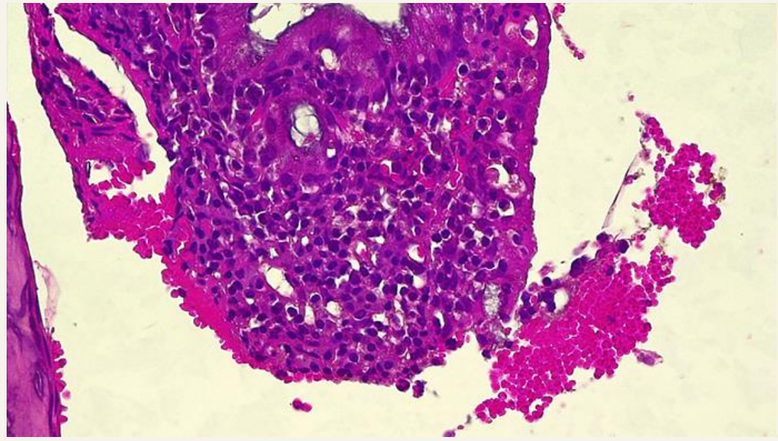
Caspase Levels and Nasal Epitelial damage score



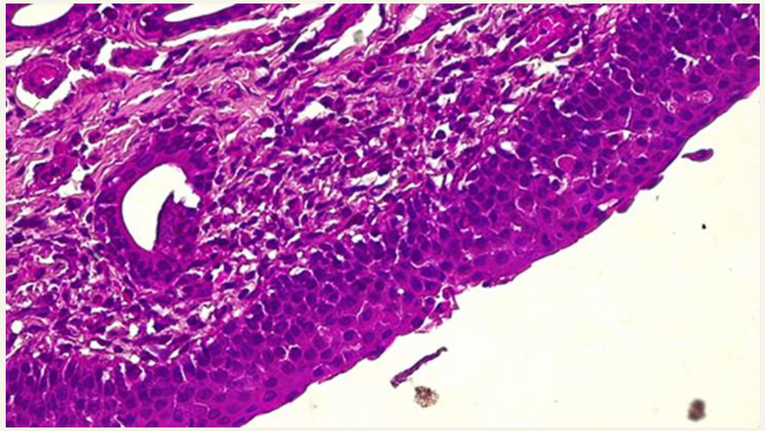




Red arrow: epithelial degeneration
Blue arrow: squamous metaplasia



Necrosis and Hemorrhage



Hyperplasia

SOD LEVELS

CSE group > Vit C group

- The CSE components are more complete than Vit C.
- Brazilin, minerals (SOD enzyme co-factor), Vitamins

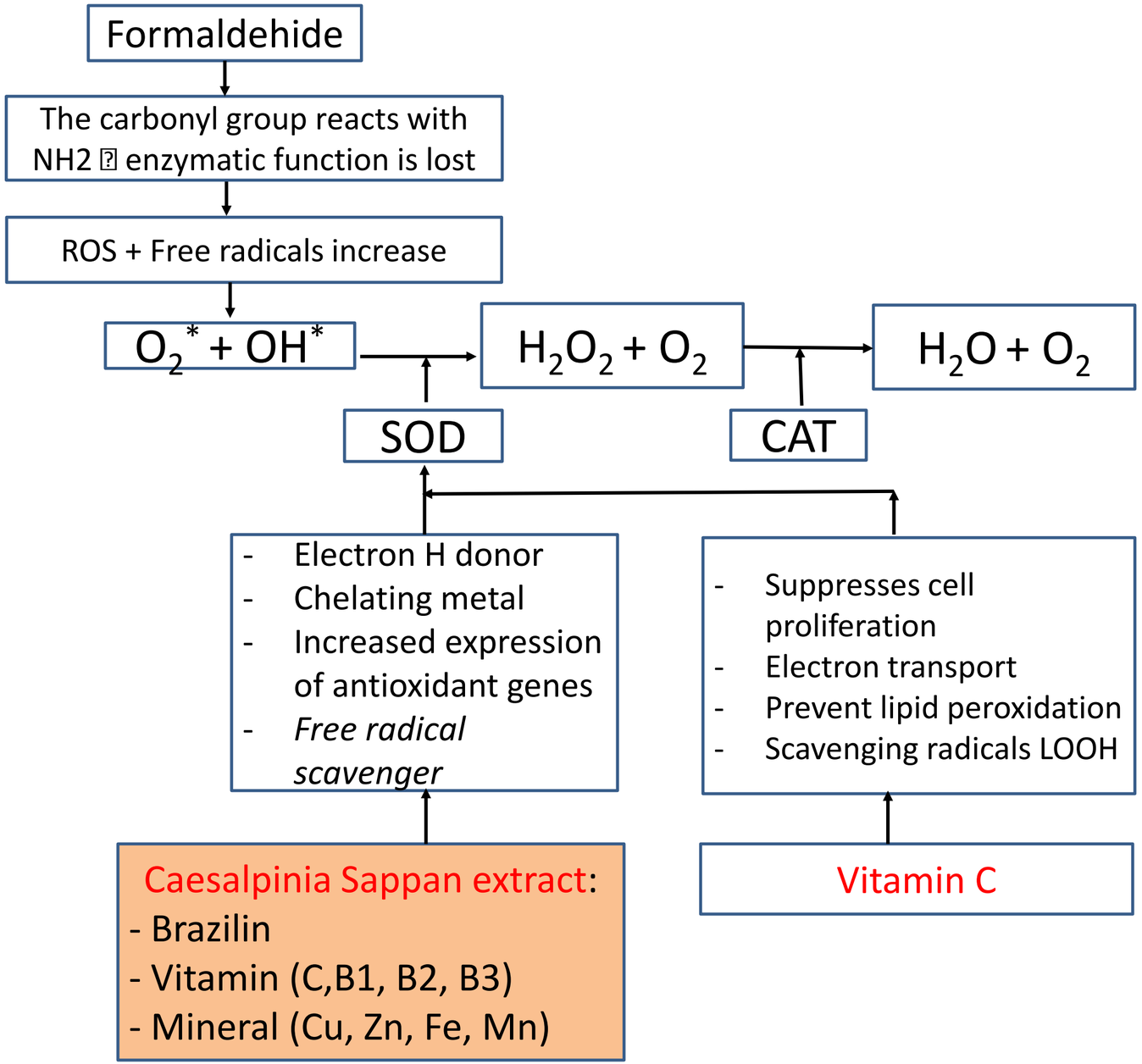
CSE group > negative group

- CSE donates H atoms
- CSE binds ROS-forming metals
- CSE inhibits enzymes that form ROS
- CSE increases endogenous antioxidant gene expression through NRF2 activation

CSE group = normal group

- CSE fights free radicals.
- CSE maintained SOD levels comparable to normal mice that did not fight free radicals.

SOD LEVEL



No proven dose-response relationship due to:

Cytotoxic effects Reducing the work of intracellular antioxidant glutathione (GSH) Gradual pharmacological response

MDA LEVEL

→ All doses of CSE and vit C were almost equally effective during the 28 days of intervention.
→ Measurement of MDA levels is not at the location of contact between formaldehyde and the body.
→ inhaled formaldehyde damages cell membranes.

CSE group > Vit C group:

Vit C binds lipid hydroperoxides at the termination stage

→ Vit C is better at suppressing fat peroxidation (MDA formation)

CSE group < negative group:

- The negative group does not receive exogenous antioxidants → oxidative stress.
- CSE scavenges free radicals and increases SOD synthesis
- CSE reduces the formation of nitric oxide (a trigger for inflammation and fat peroxidation)

MDA at CSE Group < MDA normal group:

oxidants are formed from normal respiration and metabolism

MDA LEVEL

Initiation Stage :

$-CH_2- + OH \rightarrow -CH- + H_2O$

$R-CH + R-CH \rightarrow R-CH-CH-R$

Propagation Stage :

$R-CH + O_2 \rightarrow ROO$

$ROO + CH \rightarrow ROOH + C$

$ROO + CH \rightarrow LOOH + C$

Termination Stage :

$LOOH \rightarrow CH_2(CHO)_2$ (MDA)

Vit C

There is a significant relationship between SOD levels and MDA levels (p=0.02 and r= -0.422)

→ SOD is used to fight oxidative damage due to exposure to formaldehyde gas so that the amount of MDA decreases.

→ The higher the SOD level, the lower the MDA level.

CASPASE 3 LEVEL

CSE 1000 group = Vit C group

- CSE prevents oxidative stress, prevents chromosome damage, activates P53, arrests incorrect cell cycle, and activates caspase 9.
- Vitamin C prevents oxidative stress.
- → the same ability because both work directly at the stage of preventing oxidative stress.

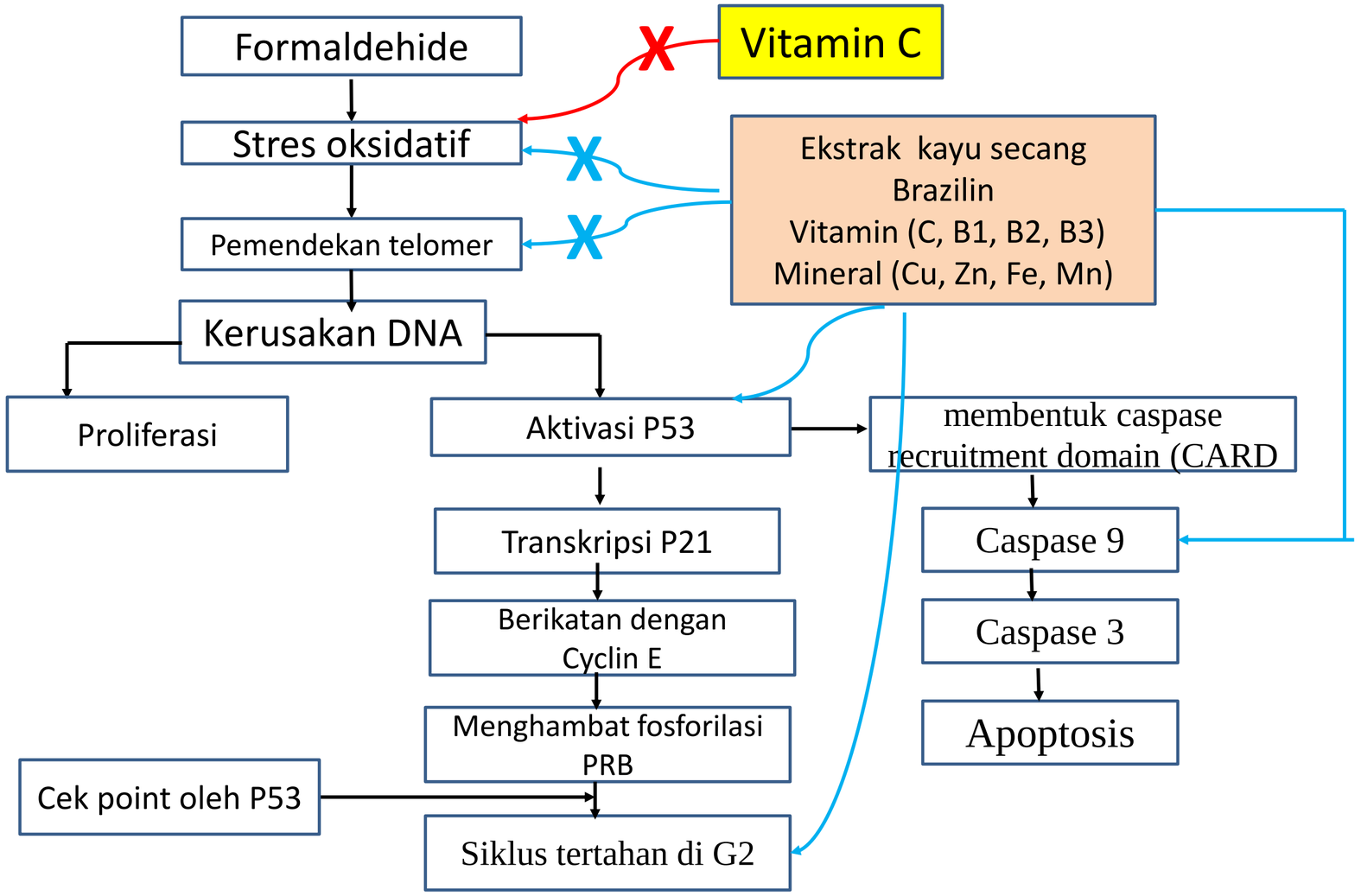
CSE group 1000 < negative group

- CSE scavenge free radicals, so there is no disruption to mitochondria as the main target of formaldehyde.

EKS group <normal group:

- CSE is able to scavenge free radicals → and reduce oxidative stress.
- Normal mice undergo physiological phenomena to maintain cell safety.

Caspase 3 Level



Descriptively:

The higher the dose of sappanwood extract, the lower the level of caspase 3.

Nasal Epithelial Damage

CSE 1000 group = Vit C group

→ CSE performance has been done by inhibiting the production of NO which causes inflammation

→ Vitamin C does not work to prevent inflammation but suppresses cell proliferation.

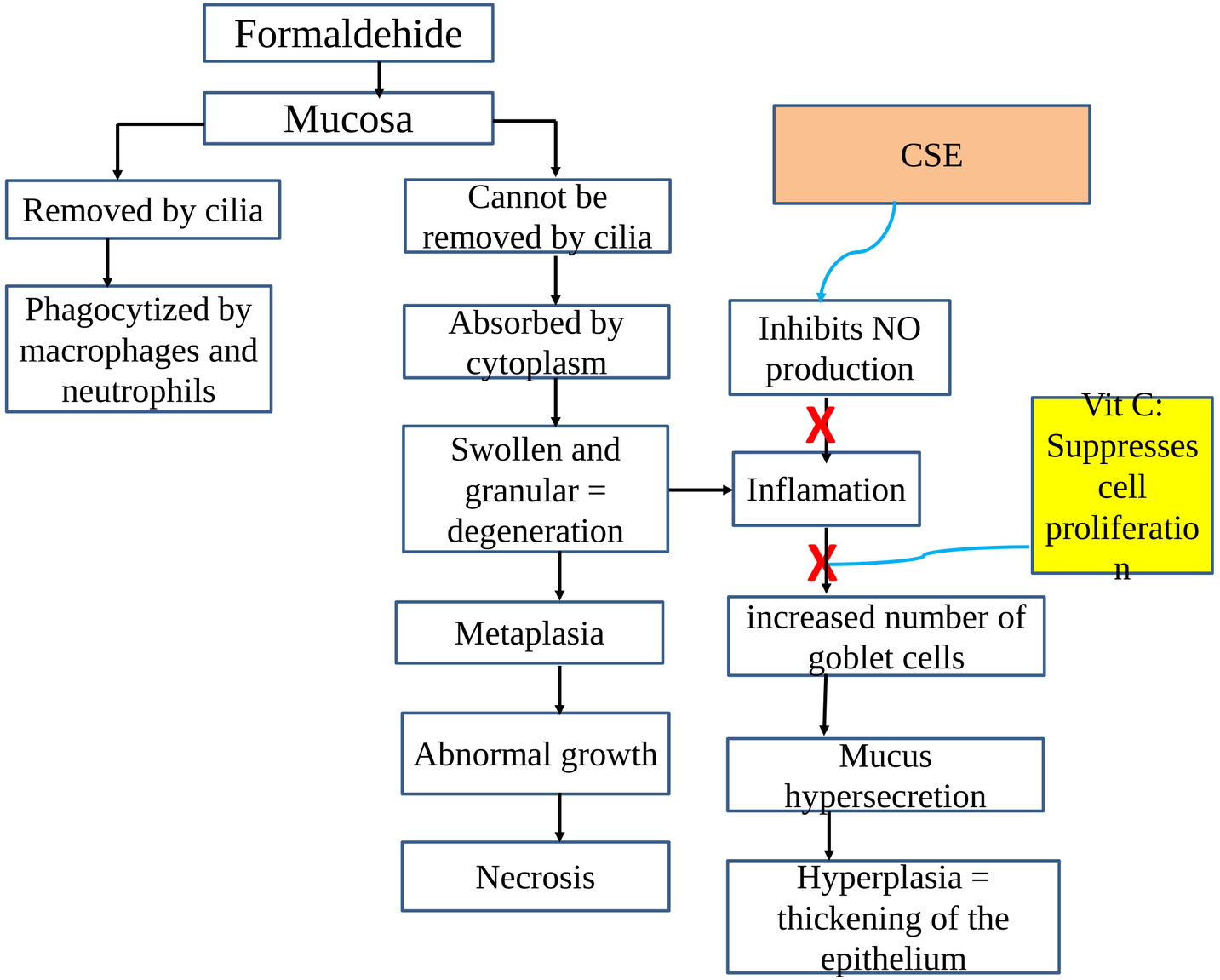
CSE group 1000 < negative group

- CSE inhibits free radical oxidation reactions cell damage can be inhibited
- The negative group did not receive antioxidant defense.

CSE group =normal group:

- CSE is able to scavenge free radicals, thereby suppressing cell damage, comparable to mice that did not receive free radicals.

Nasal Epithelial Damage



Descriptively:
The dose response relationship of giving sappanwood extract to nasal epithelial cell damage has emerged, but the difference is not significant.

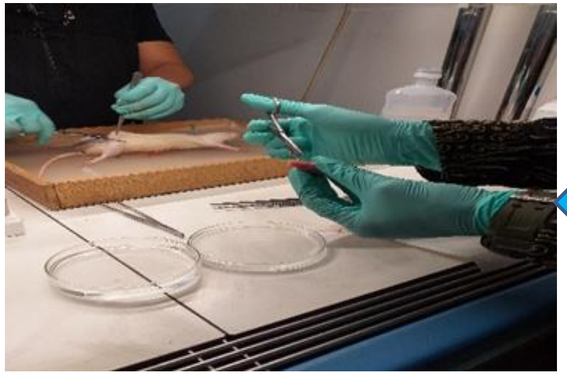
From the results of this study, it is proven that CSE can prevent cell damage through increasing endogenous antioxidants and preventing lipid peroxidation in experimental animals.

Thus, natural materials such as CSE can be used as candidates for preventing diseases caused by exposure to toxic materials







THANK YOU