

# **Bacopa monnieri-induced Protective Autophagy Inhibits Benzo[a]pyrene-Mediated Apoptosis**

**Dr. Sujit kumar Bhutia**  
**Associate Professor**

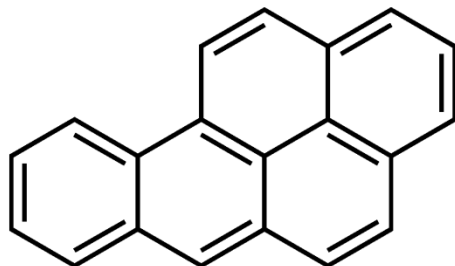
**Department of Life Science**  
**National Institute of Technology**  
**Rourkela**



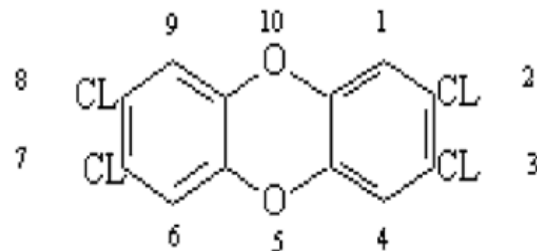
# AIR POLLUTION

- ❖ **Air pollutants – Major problem of developing industrial cities like Rourkela**
- ❖ **Particulate matter (PM) – forms a mixture of inorganic and organic component that vary in size, origin and composition :**
  - Coarse PM (2.5-10  $\mu\text{m}$ )**
  - Fine PM (0.1 – 2.5  $\mu\text{m}$ )**
  - Ultrafine PM (<0.1  $\mu\text{m}$ )**
- ❖ **Industrial PM contains organic volatile polycyclic aromatic hydrocarbon like Benzo[a]pyrene, anthracene, 1, 2-Benzpyrene, Dioxin, Dibenzofuran**
- ❖ **Benzo[a]pyrene, Dioxin - most potent pollutant assessed by Environmental Protection Agency (EPA)**
- ❖ **Major PM source : Industries, Power plant, Incinerators, Constructions**
- ❖ **Cause: Increased mortality, morbidity including increased risk of cancer among industry workers**

# BENZO[A]PYRENE



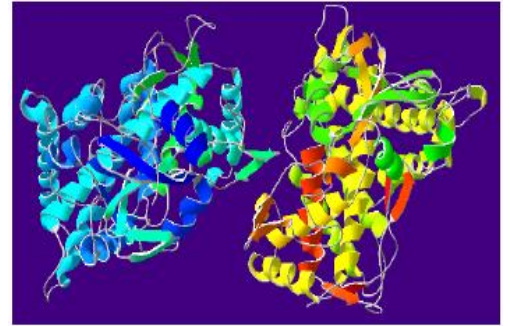
# DIOXIN



- ❖ Benzo[a]pyrene, Dioxin- Group 1 carcinogen (IARC)
- ❖ Cytochrome P450 inadvertently converts a precarcinogen like Benzo[a]pyrene and Dioxin- into highly potent carcinogens leading to widespread **CANCER!**

# CYTOCHROME P450

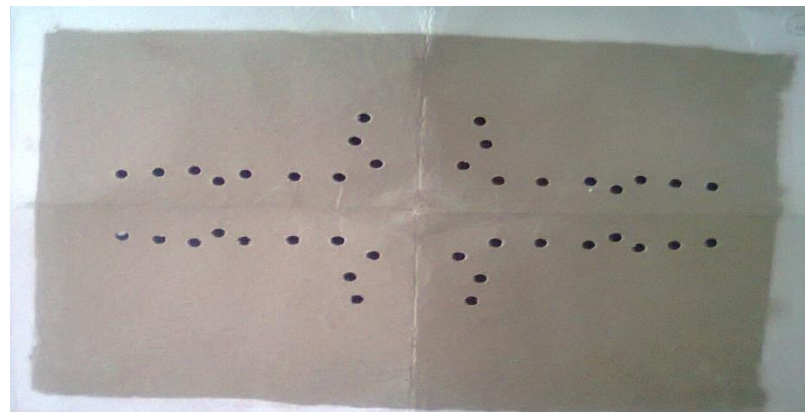
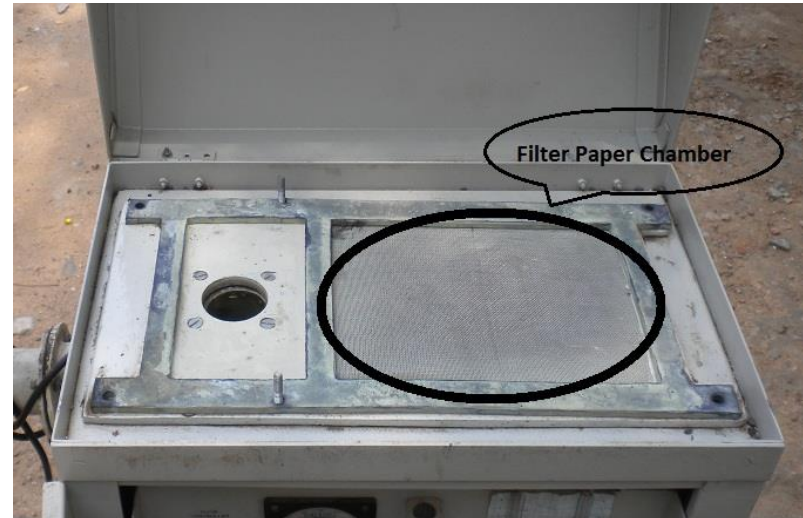
- ❖ **Cytochrome P450 superfamily (CYP)**
  - large diverse group of enzymes



- ❖ **Human CYPs** - membrane associated proteins located either in inner membrane of mitochondria or in endoplasmic reticulum of cells
- ❖ **Cytochromes P450 (CYPs)** belong to superfamily of proteins containing heme cofactor
- ❖ **Most common reaction catalyzed by cytochromes P450 is monooxygenase reaction, where one atom of oxygen is inserted into an organic substrate (RH) while the other oxygen atom is reduced to water:**

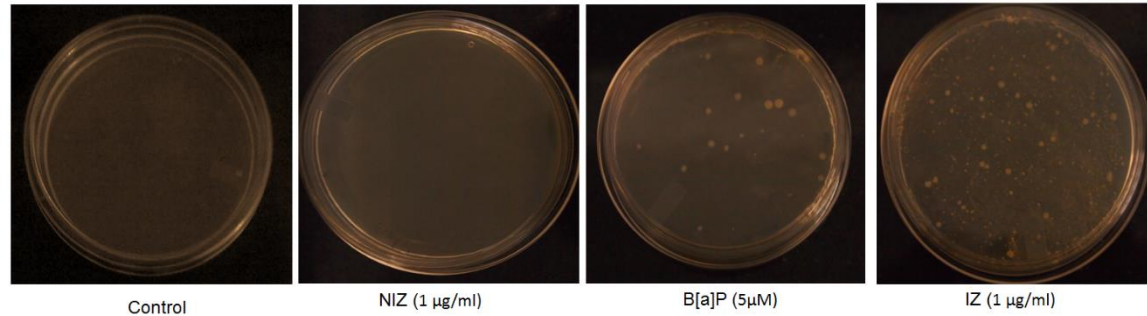


# Analysis of particulate matter collected from Rourkela city

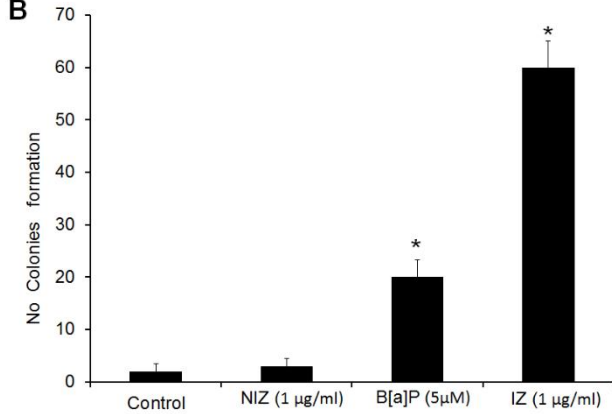


# Analysis of PM collected from Rourkela city

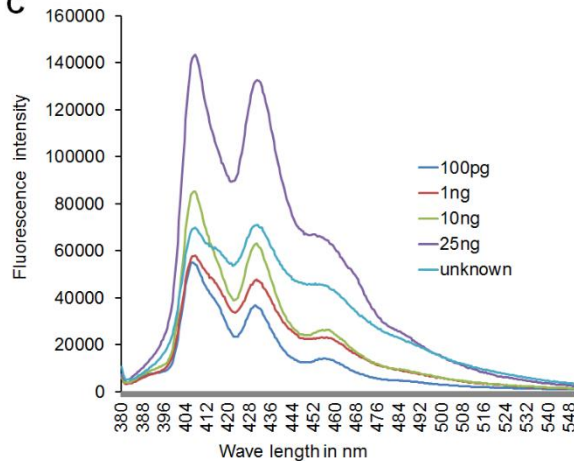
A



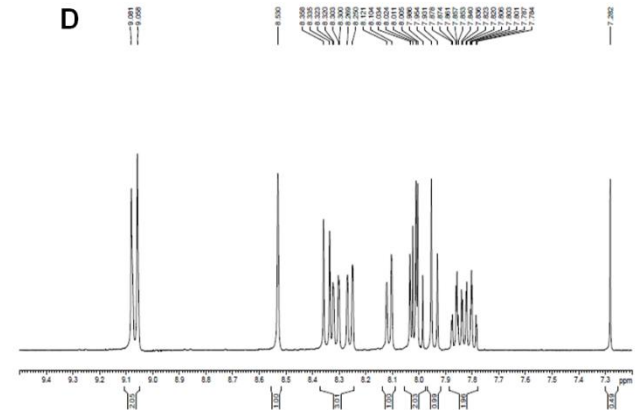
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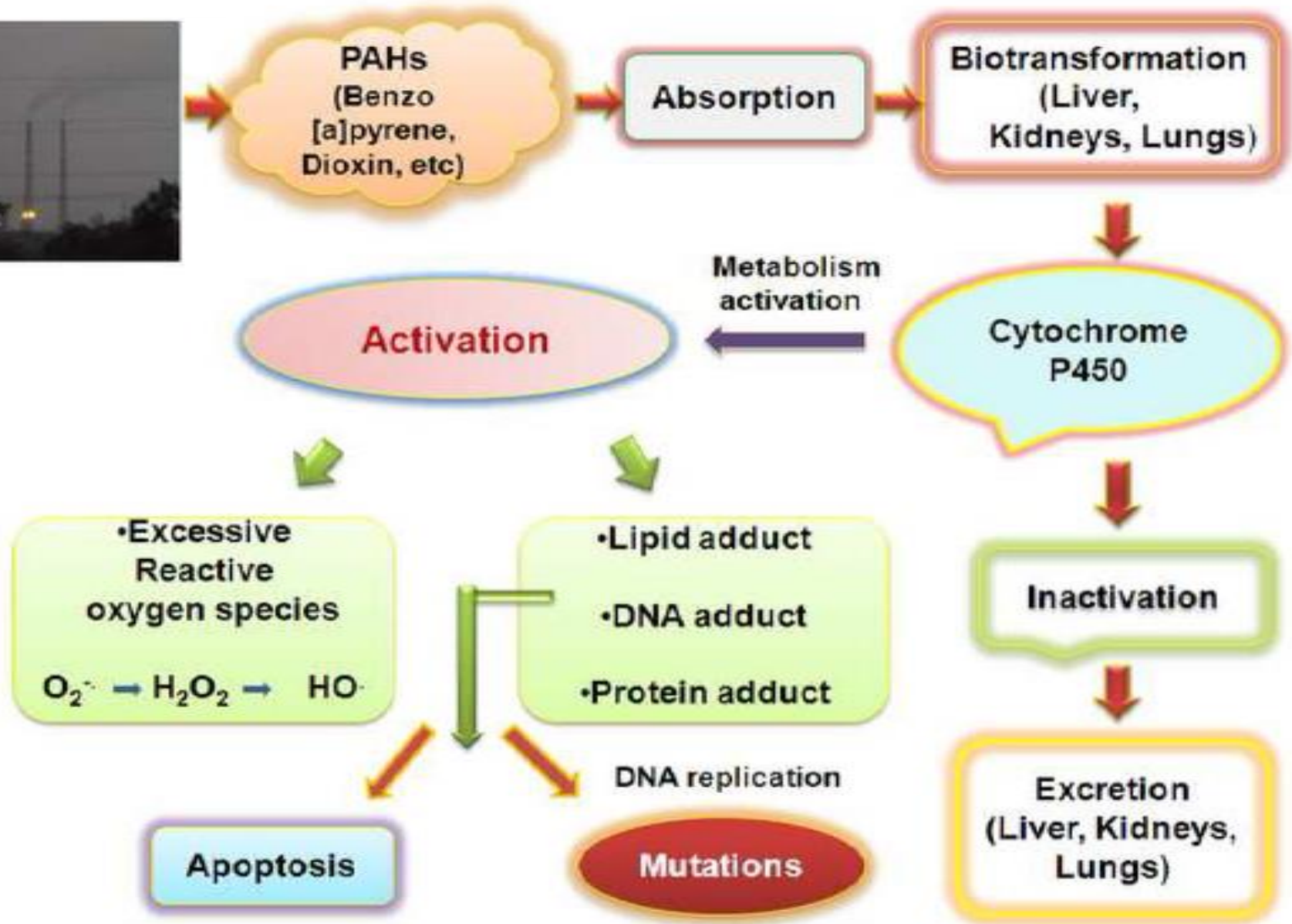
C



D







**Necrosis:** a pathological response to cellular injury



Chromatin clumps

Mitochondria swell and rupture

Plasma membrane lyses

Cell contents spill out

General inflammatory response is triggered

**Apoptosis:** a physiological response to specific suicide signals, or lack of survival signals



Chromatin condenses and migrates to nuclear membrane. Internucleosomal cleavage leads to laddering of DNA at the nucleosomal repeat length, ca. 200 bp.

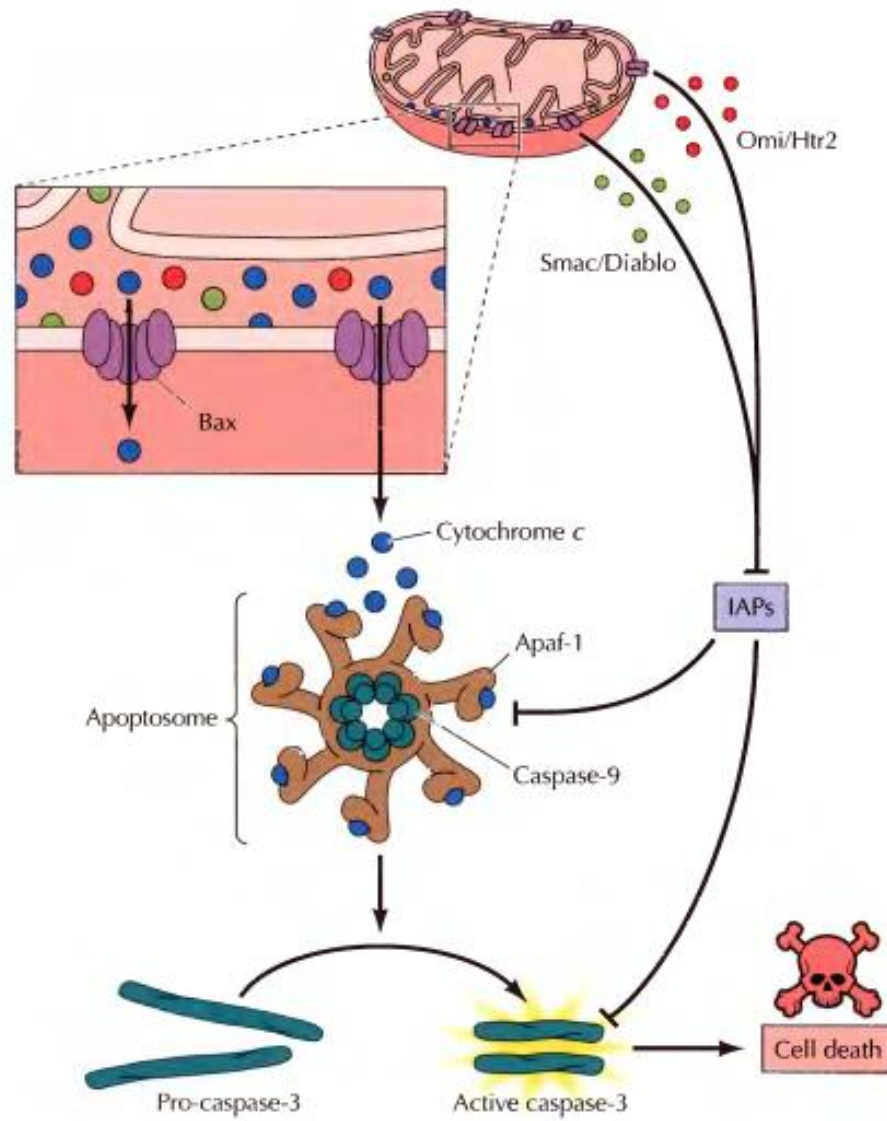
Cytoplasm shrinks without membrane rupture

Blebbing of plasma and nuclear membranes

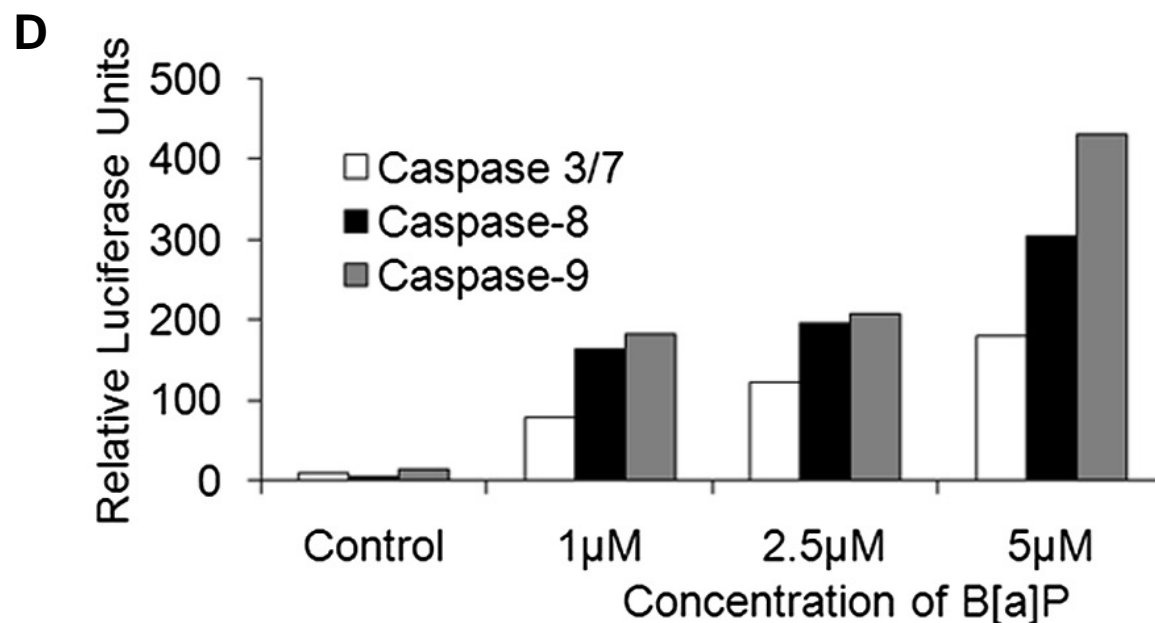
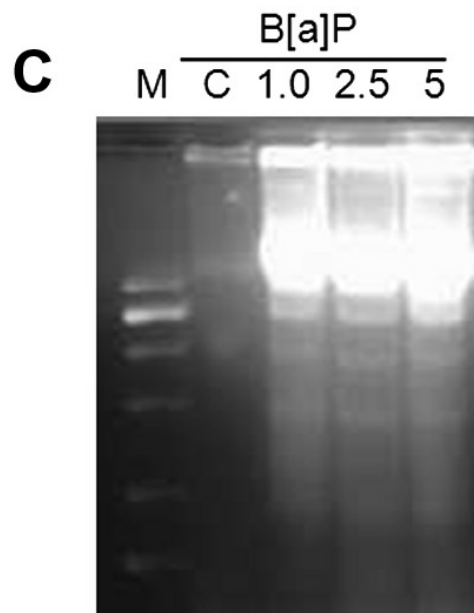
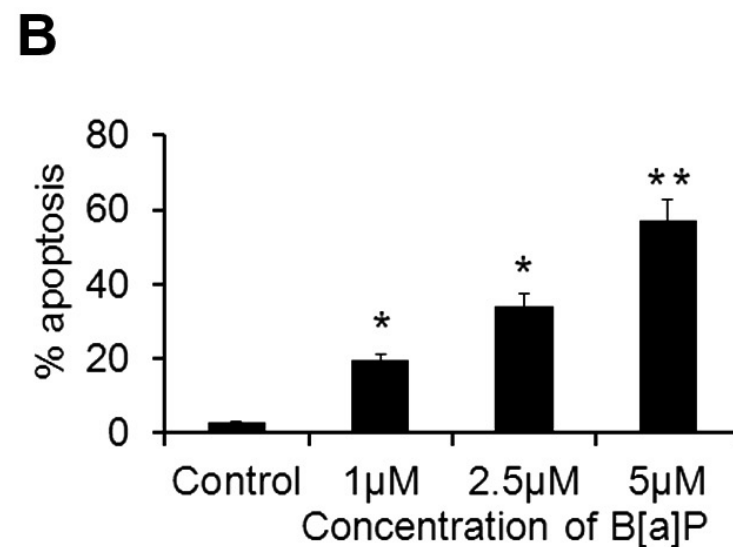
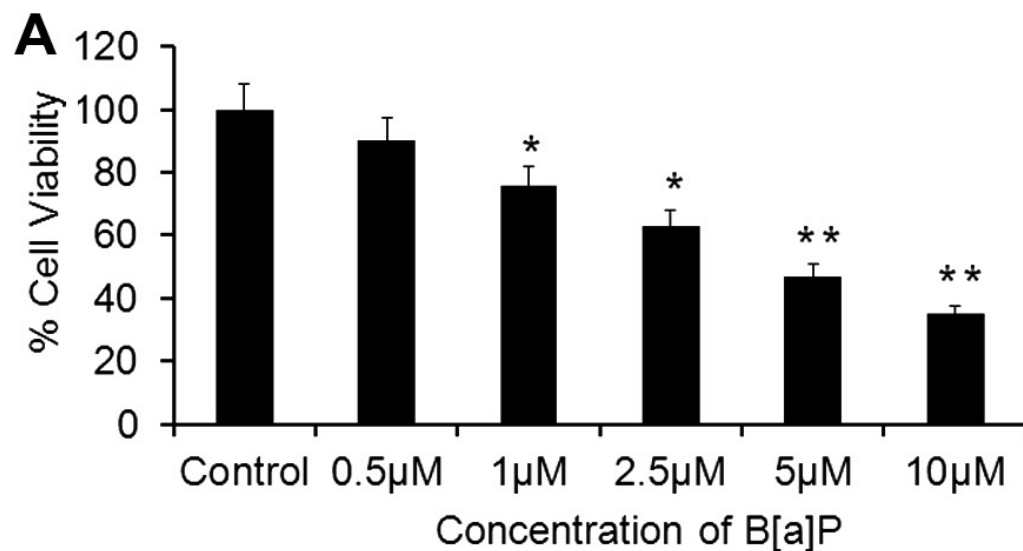
Cell contents are packaged in membrane bounded bodies, internal organelles still functioning, to be engulfed by neighbours.

Epitopes appear on plasma membrane marking cell as a phagocytic target.  
No spillage, no inflammation





# Benzo[a]pyrene induces apoptosis

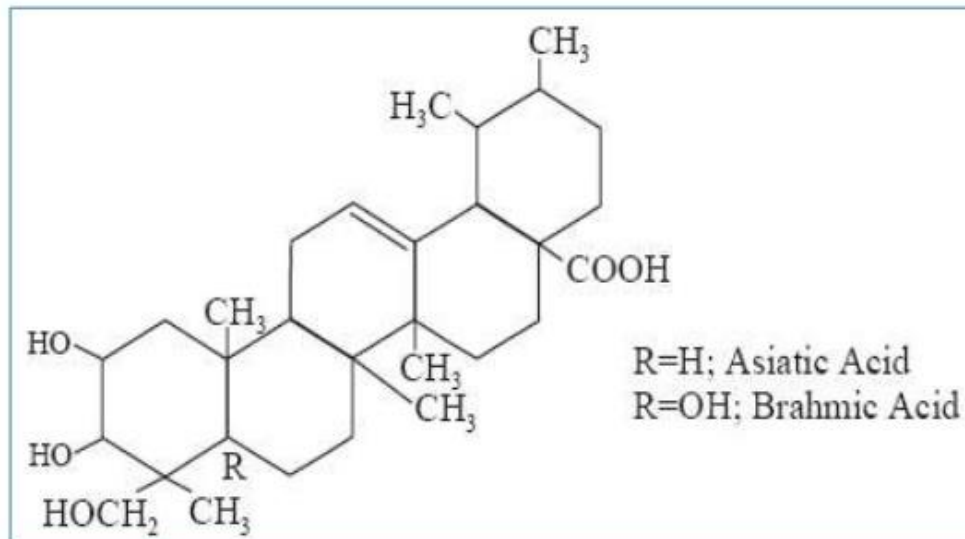


## BACOPA MONNIERI

Synonyms Herpestis; Brahmi.

**Biological Sources:** It comprises of the fresh stems and the fresh leaves of *Bacopa monnieri* belonging to family *Scrophulariaceae*.

**Chemical Constituents:** The leaves contain saponin glycosides known as Bacoside-A and Bacoside-B which on acid hydrolysis give rise to triterpenoid aglycone termed as bacogenin-A and Bacogenin-B respectively. It also contains Asiatic acid and Brahmic acid



## MEDICINAL USES

BM has been studied extensively in animal models and *in vitro*. While BM is implicated in the treatment of anxiety, epilepsy, and other neurodegenerative disorders,

Bacopa monnieri, known to most as Brahmi, acts as an adaptogen; which means it helps the body adapt to new or stressful situations

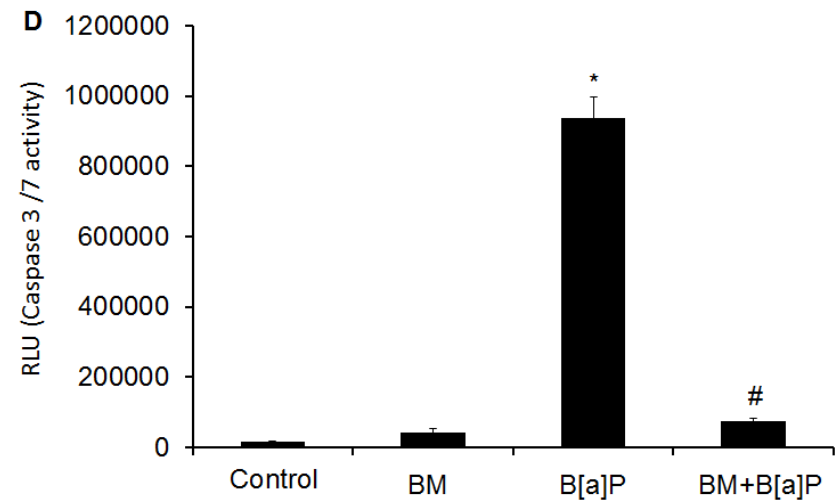
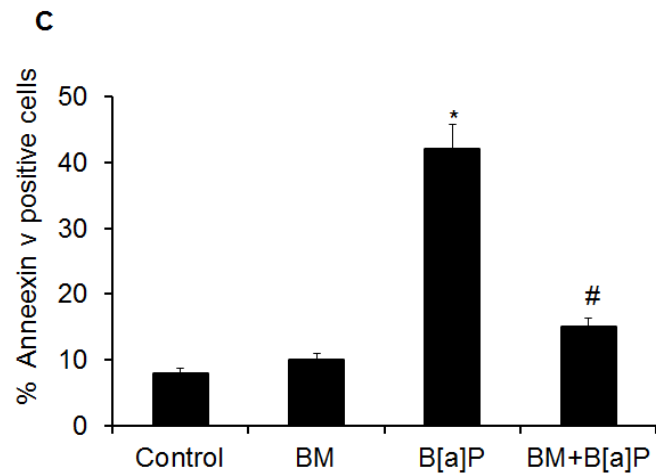
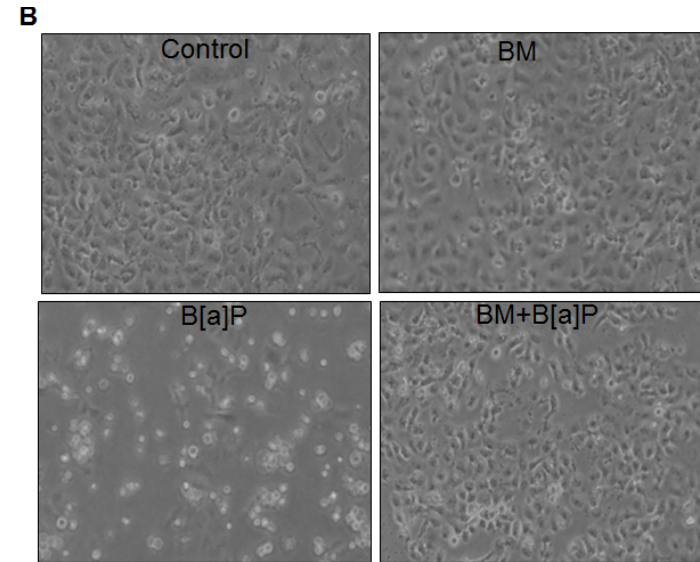
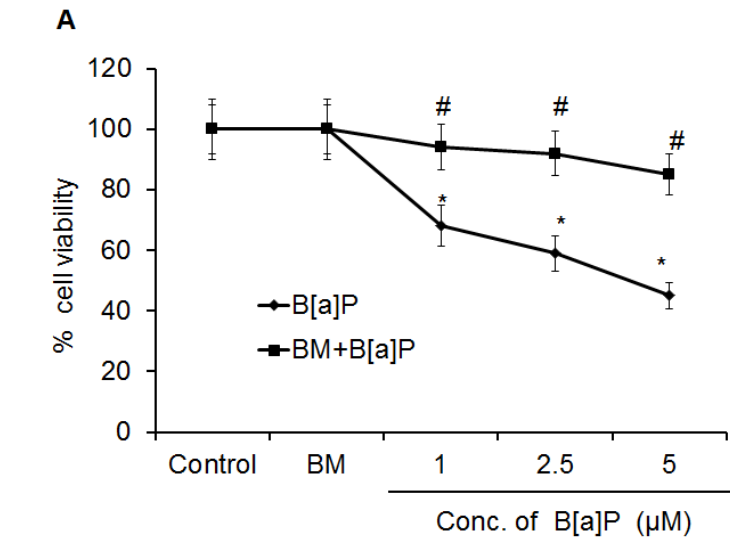
Although Bacopa has been indicated as a remedy for epilepsy in Ayurvedic medicine, research in animals shows anticonvulsant activity

Animal studies have demonstrated Bacopa extracts have a relaxant effect on chemically-induced broncho-constriction.

Use of Bacopa as a “cardiotonic” is frequently mentioned in Ayurvedic medicine.

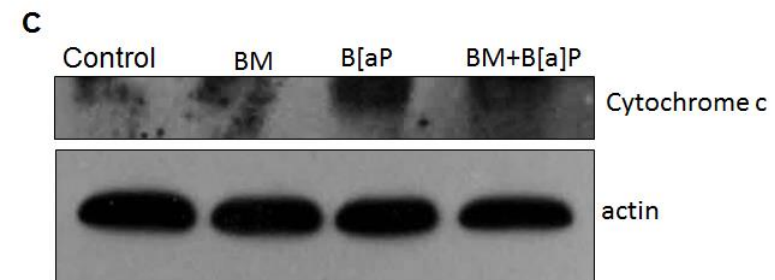
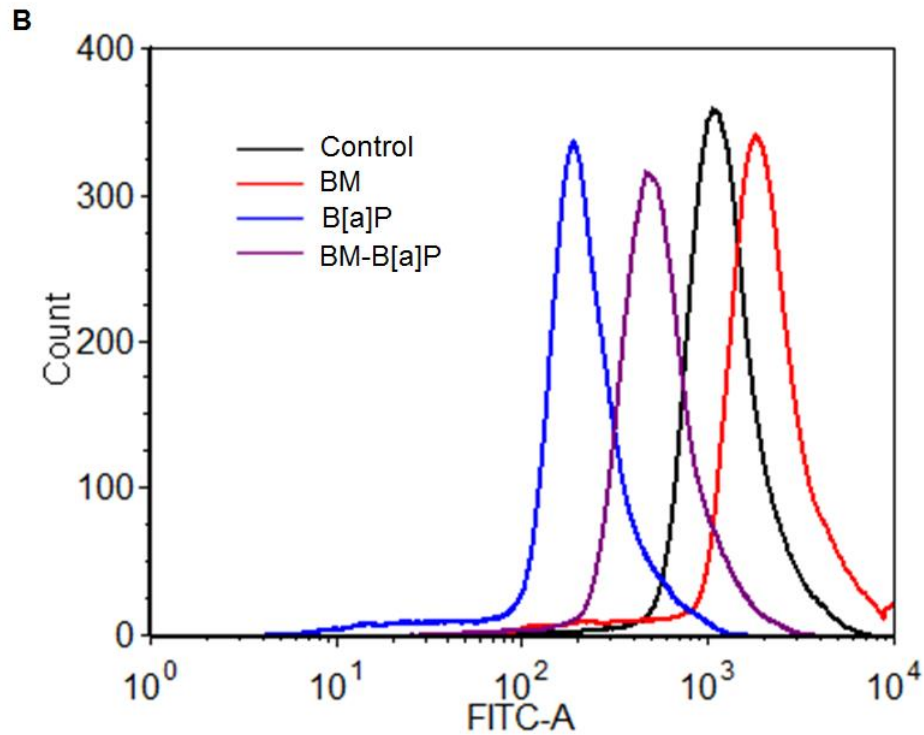
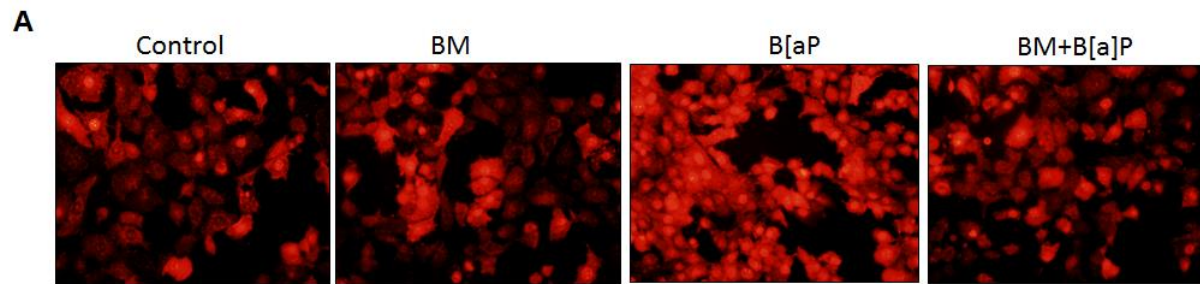
A study in mice demonstrated high doses (200 mg/kg) of Bacopa extract increased the thyroid hormone,

# Bacopa monnieri found to protect benzo[a]pyrene-induced cytotoxicity in HaCaT cells





## BM diminish B[a]P-induced mitochondrial dysfunction

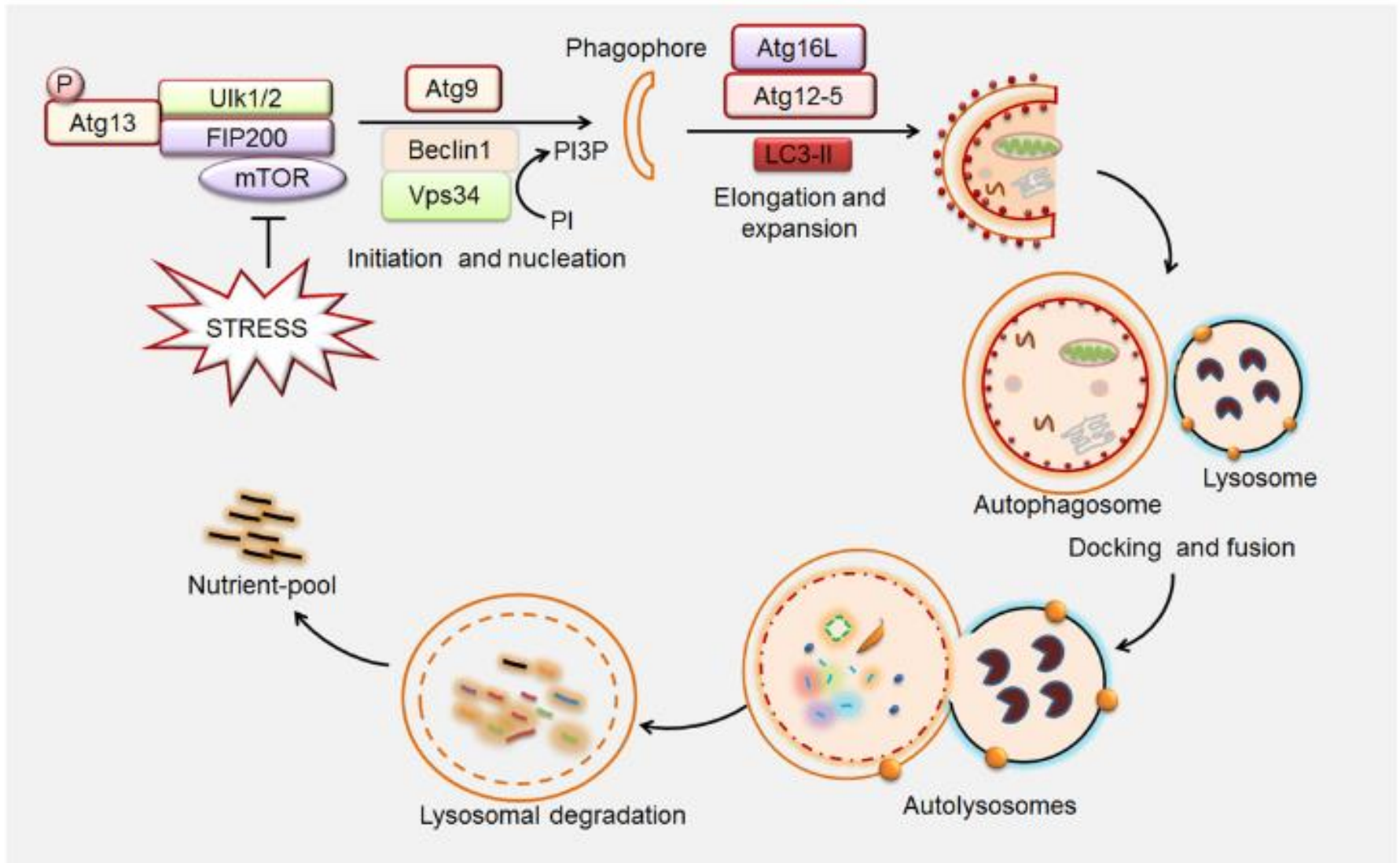




# Autophagy

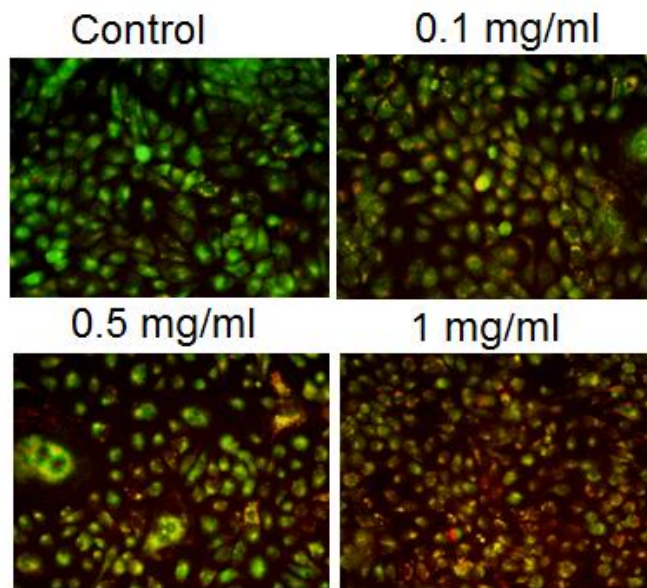
- ❑ Autophagy “eat onself”
- ❑ Highly **conserved** and **regulated** catabolic process that maintains **cellular homeostasis**
- ❑ Protect cells against **starvation**, **microbe invasion**
- ❑ Repair mechanism
- ❑ Programmed cell death-II

# Autophagy: The self degradation process

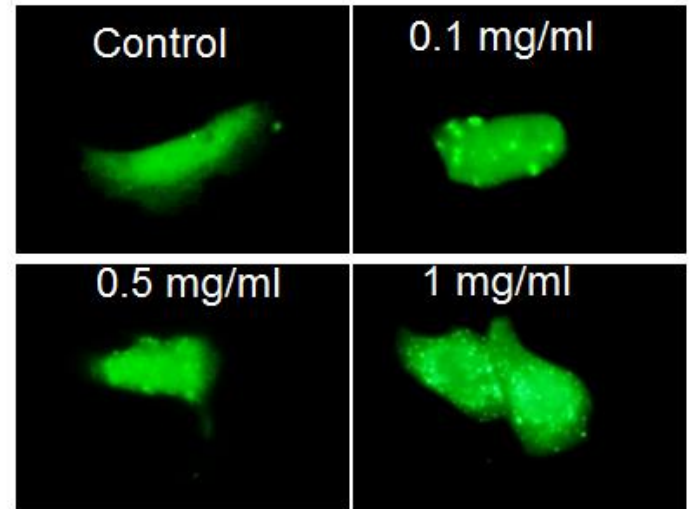


# Autophagy induction by BM in HaCaT cells

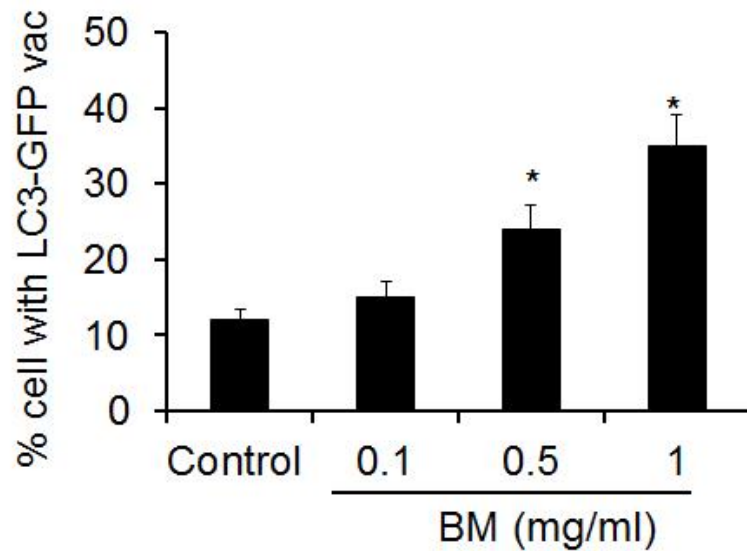
**A**



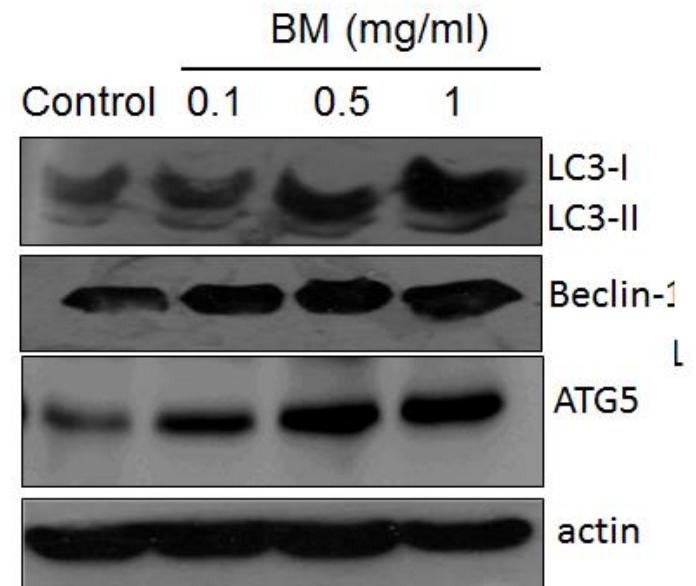
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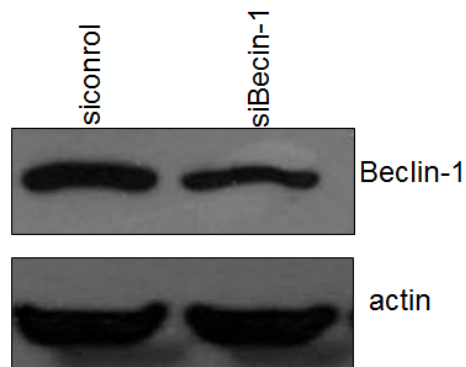
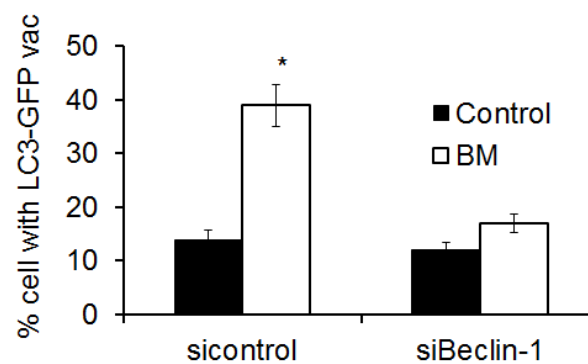
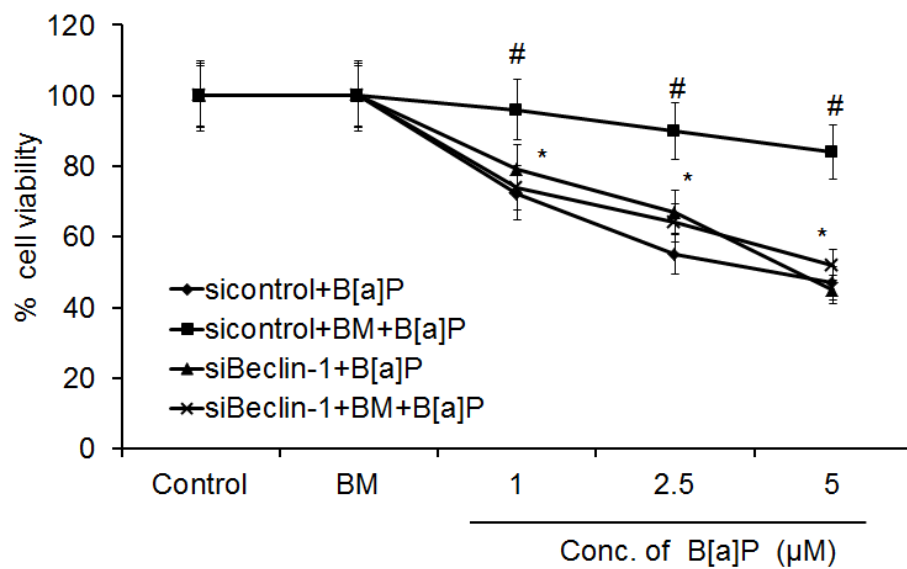
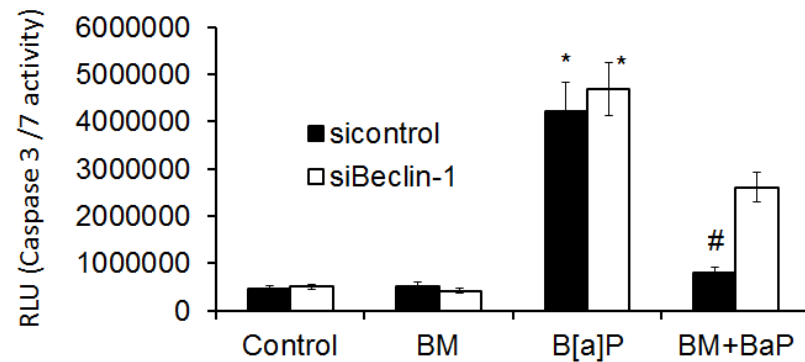


**C**

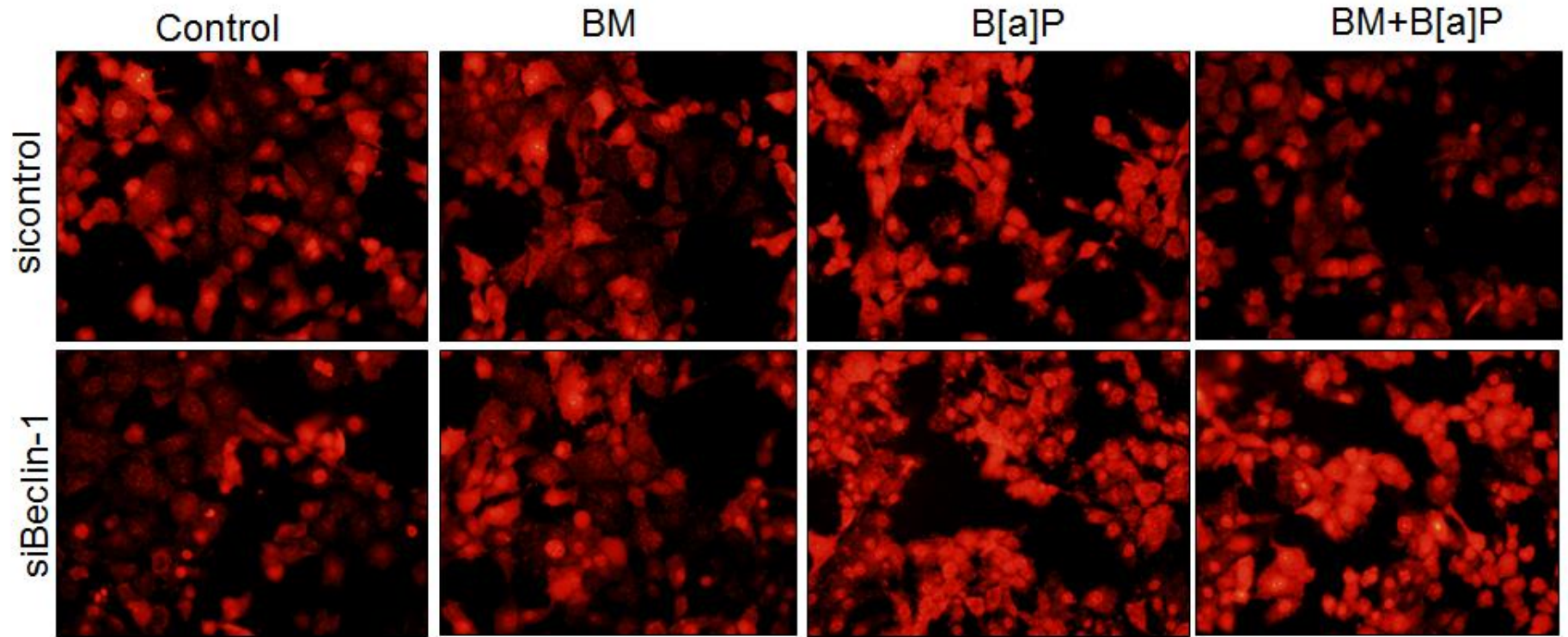


**D**



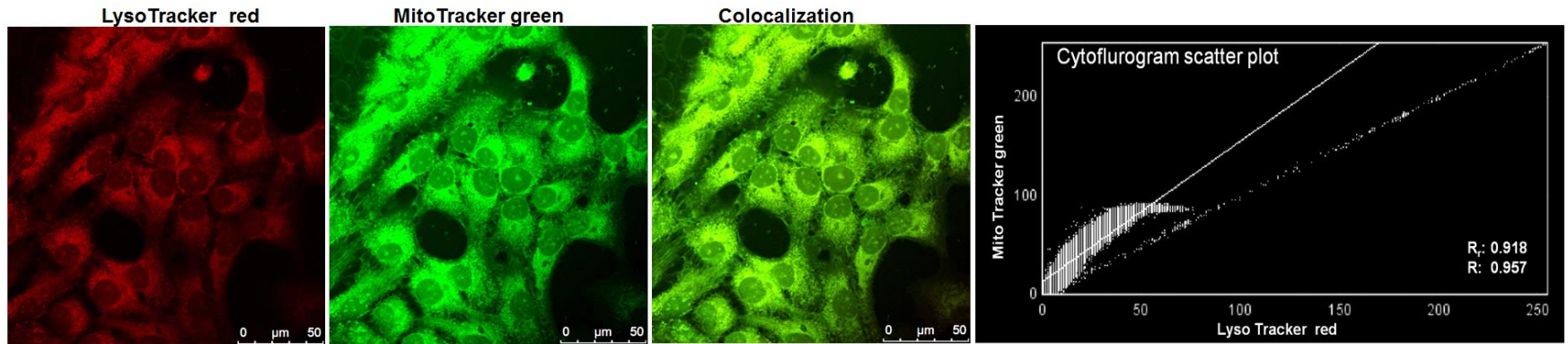
**A****B****C****D**

# Role of BM in mitochondrial ROS generation by B[a]P in Beclin-1-deficient HaCaT cells



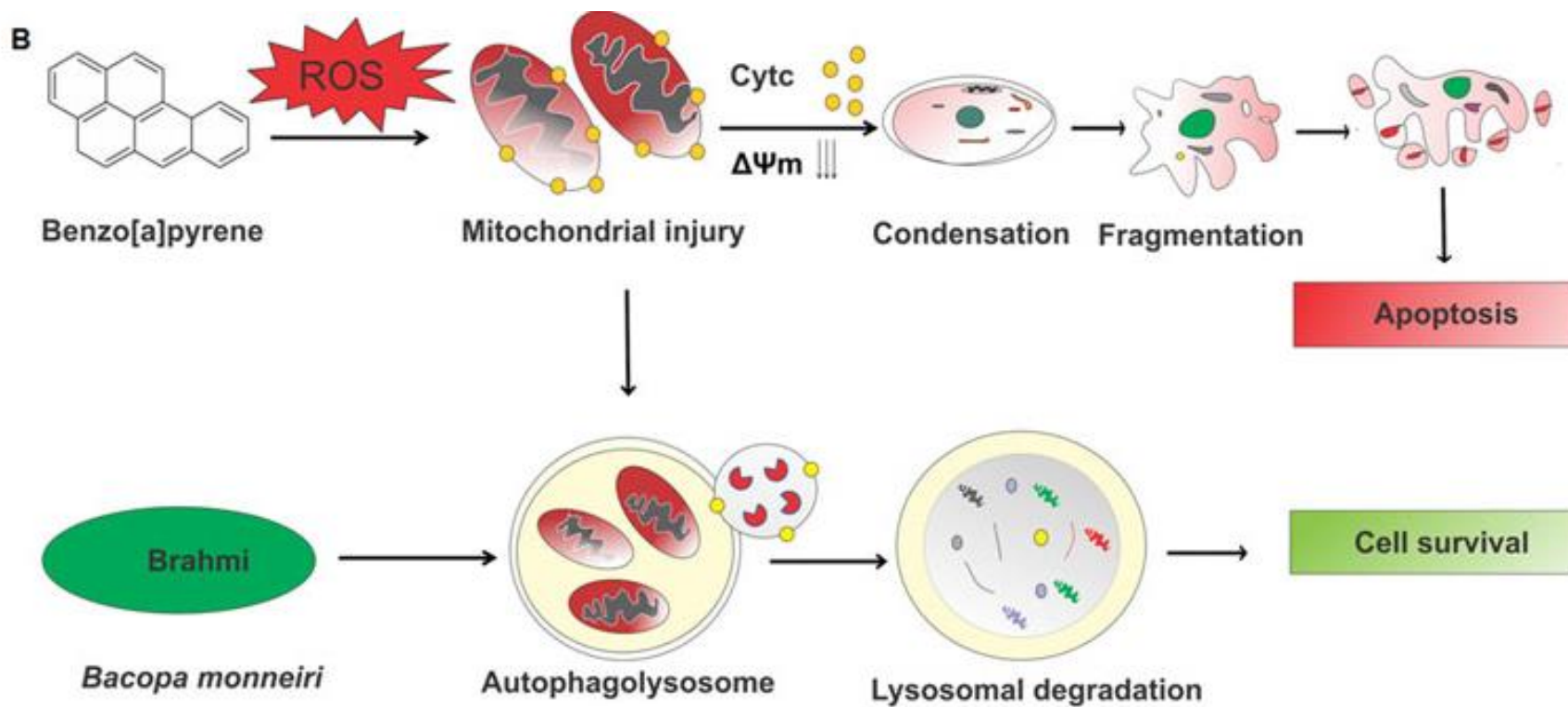


B[a]P-induced reactive mitochondria were cleared by BM-promoted autophagy





## Summary





**THANK YOU**