

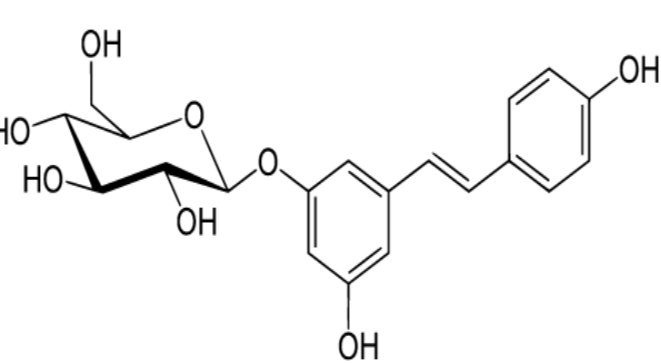
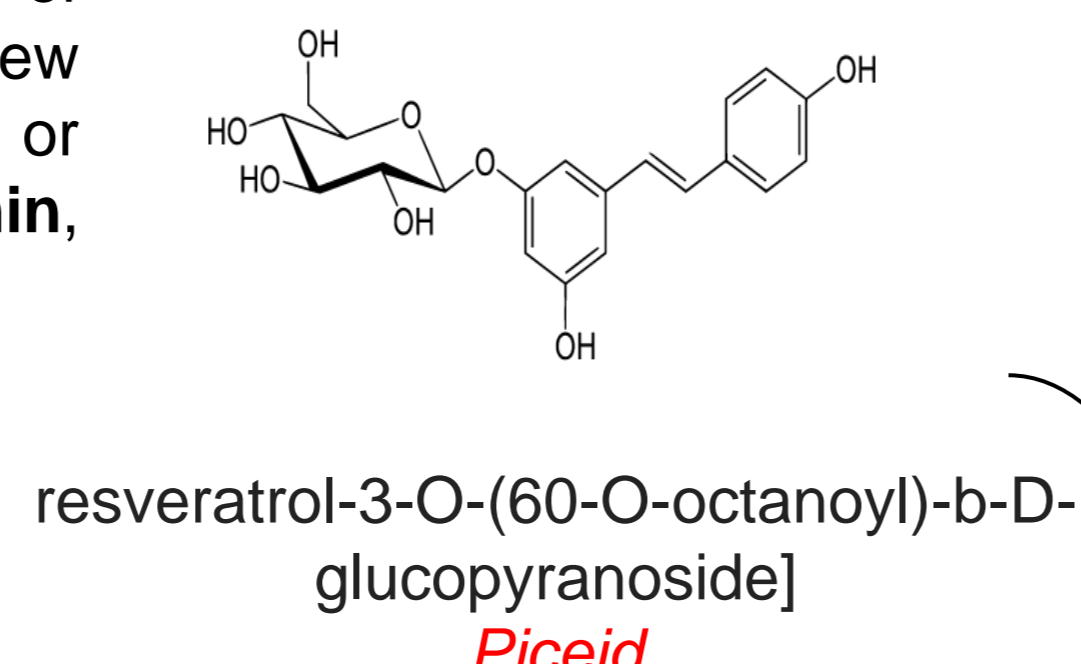
AVAILABLE APPROACHES FOR OVERCOMING LOW BIOAVAILABILITY OF RESVERATROL

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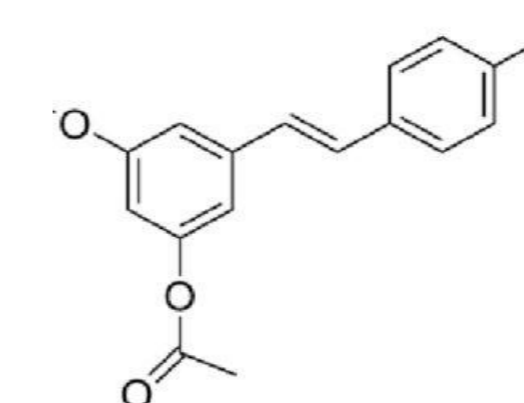
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Over the years researchers have been trying different methods aiming to overcome RSVs low water solubility: co-administration with inhibitors of glucuronidation, use of RSVs methylated analogs and designing the new delivery systems - using cyclodextrins (found in lemon juice) or endogenous proteins with high binding capacity to RSV: **serum albumin, haemoglobin, fibrinogen or LDL cholesterol**.

PRODRUGS

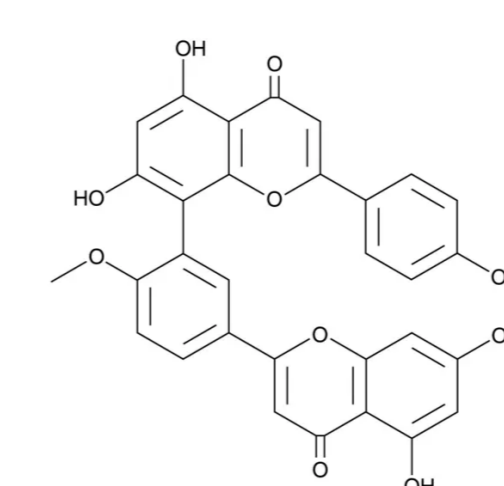


Improved treatment of neurodegeneration (Huntington's disease)



3,5,4'-tri-O-acetylresveratrol (TARES)

suppression of pulmonary inflammation and oxidative stress
increasing the concentration of free RSV

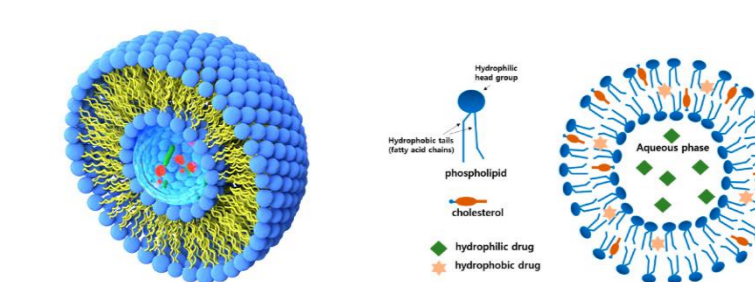


biflavone ginkgetin

SYNERGISM WITH OTHER PHYTOCHEMICAL

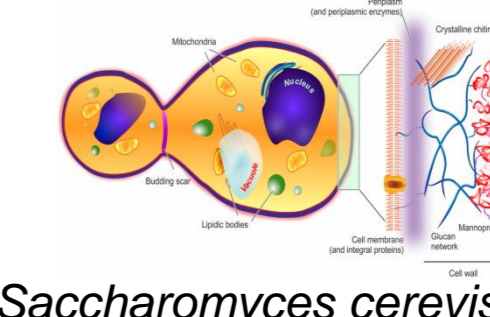
IMPROVING PHARMACOKINETICS

Formulations to improve its aqueous solubility



Liposomal RSV

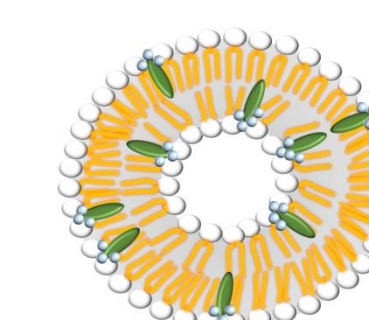
Formulations to stabilize and protect



slower photodecomposition

Formulations to achieve targeted release

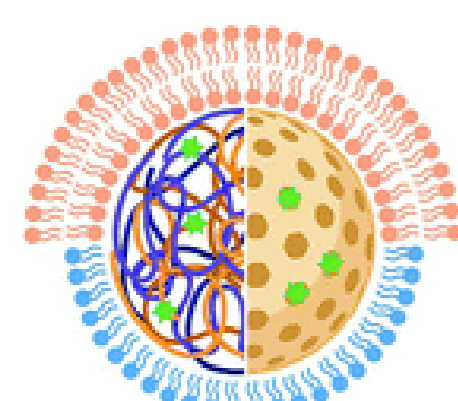
solubilize RSV most efficiently



micellar solutions of bile acids

suppression of angiogenic properties of VEGF (vascular endothelial growth factor)
reduction of TNF- α and IL-6

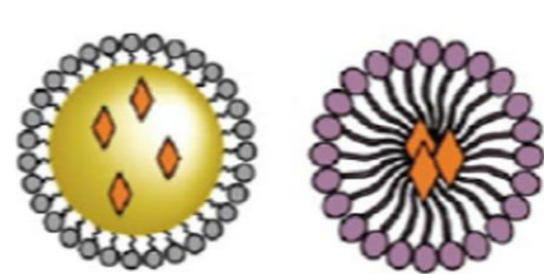
INHALATION



Dipalmitoylphosphatidylcholine-coated lipid nanoparticles (DPPC-LNs)

treatment of pulmonary arterial hypertension

TRANSDERMAL

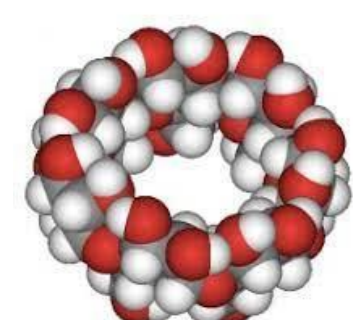


Microemulsions (Isopropyl myristate)

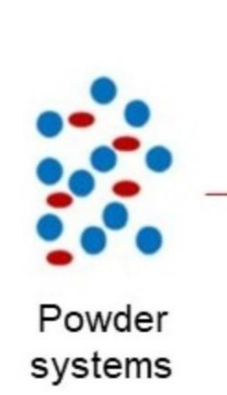
various skin conditions

ALTERNATIVE ROUTES OF ADMINISTRATION

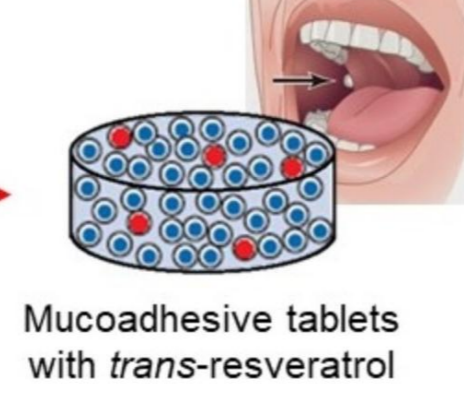
BUCCAL



β -D-Cyclodextrin



Powder systems

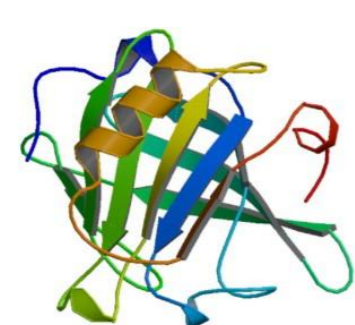


Mucoadhesive tablets with trans-resveratrol

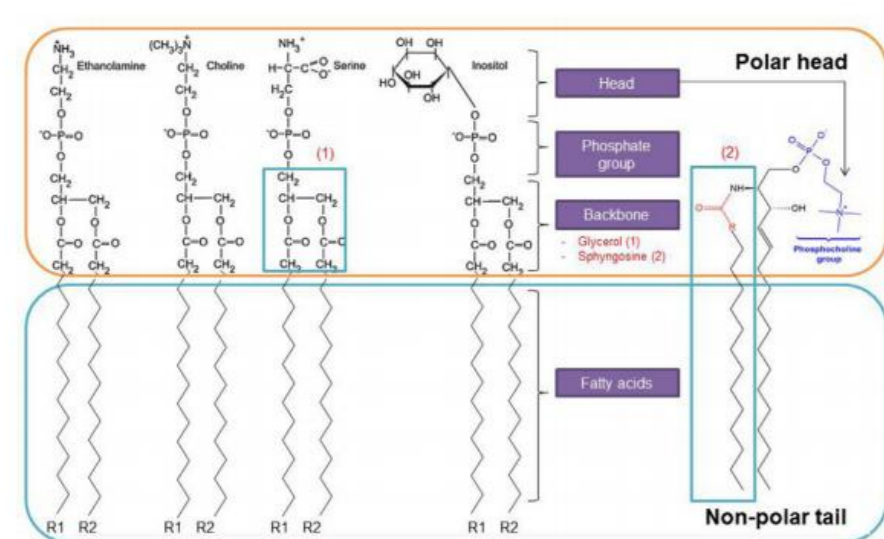
Besides, many proteins used in the food industry may serve as RSV carriers:



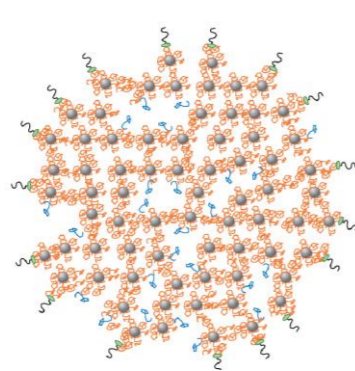
β -lactoglobulin (a major whey protein)



gliadin



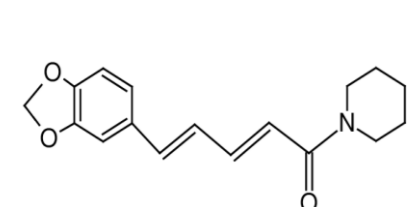
whole buttermilk



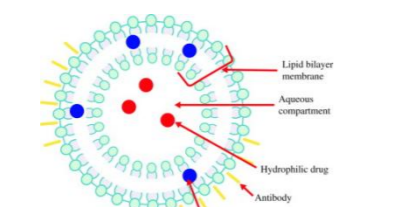
α -casein

In one study, liposomal RSV improved biochemical and histopathological alterations in doxorubicin-induced cardiomyopathy via upregulation of sarco/endoplasmic reticulum calcium ATPase2a expression. Ultra-flexible liposomes called transferosomes offer interesting delivery method that is suitable for transdermal application. Encapsulation of RSV using grape seed or orange oil, additionally, protects RSV against UV-light isomerization and degradation. It is very important to carefully monitor the dose of RSV since higher dose may cause adverse effects and lower dose may fail to exert any beneficial effect.

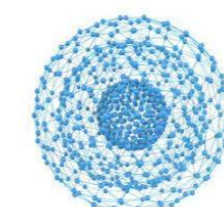
FUTURE PERSPECTIVES ?



Piperine (Inhibitor of glucuronidation)

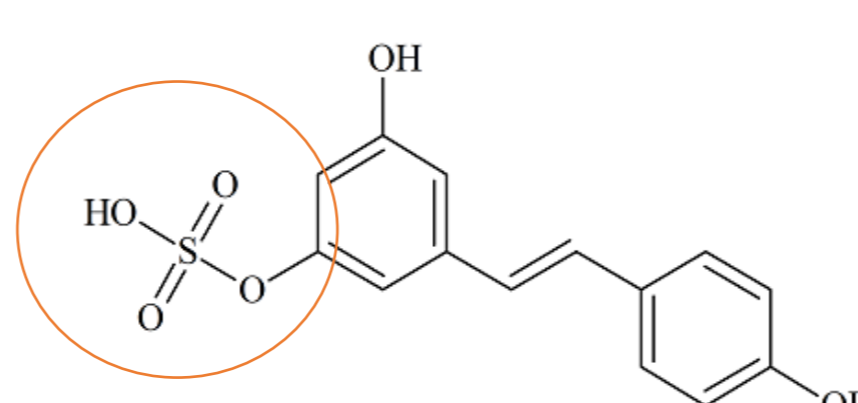


colloidal carriers in the nanometer range



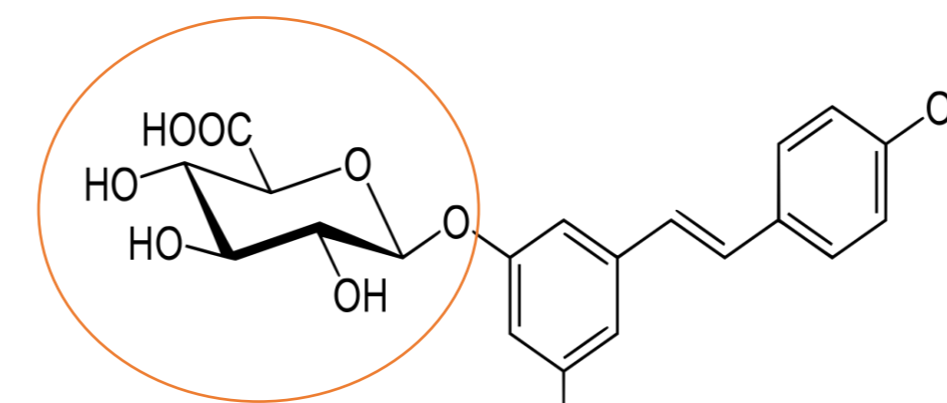
Biodegradable nanoparticles

METABOLITES



Resveratrol-3-O-sulfate

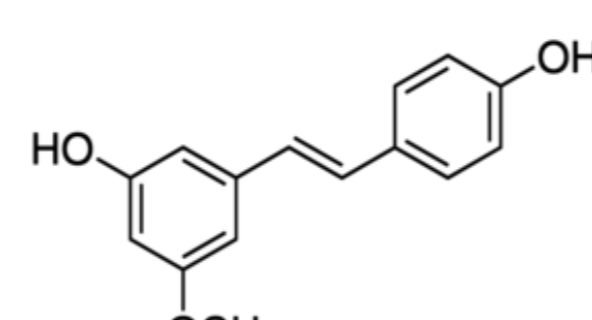
Better regulate gut microbial growth and provide superior gut barrier function



trans-Resveratrol-3-O-glucuronide

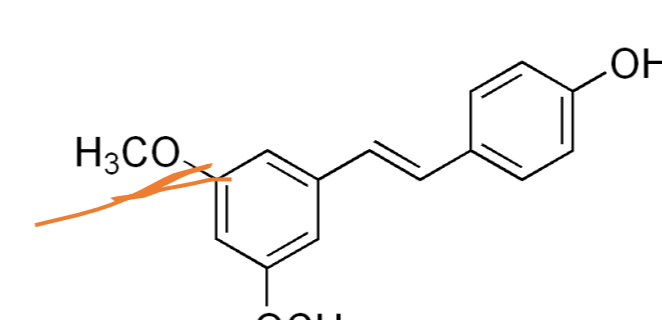
Very little activity although possesses estrogenic receptor α - antagonistic activity

NATURALLY OCCURRING RSV ANALOGUES



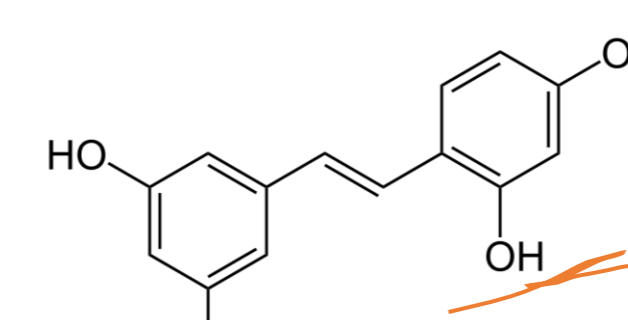
pinostilbene

Potent neuroprotective effects vs. RSV



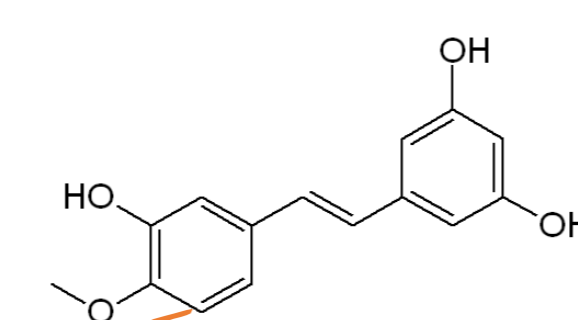
pterostilbene

Higher anti-inflammatory activity vs. RSV



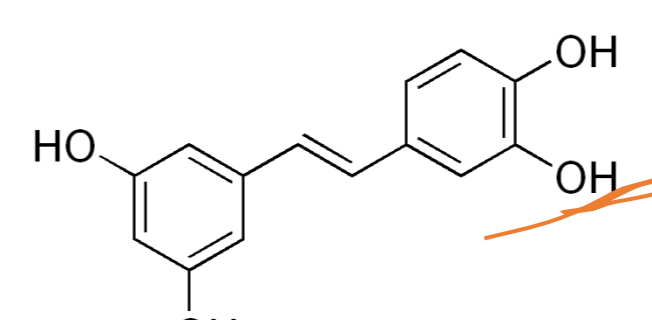
oxyresveratrol

Increase in anticancer bioactivity



rhapontigenin

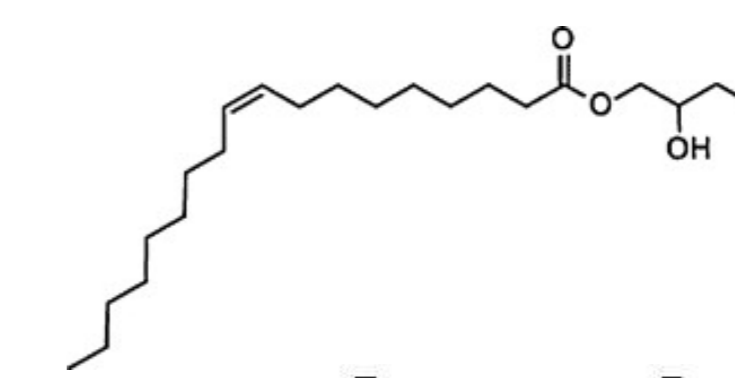
Increase in oral bioavailability



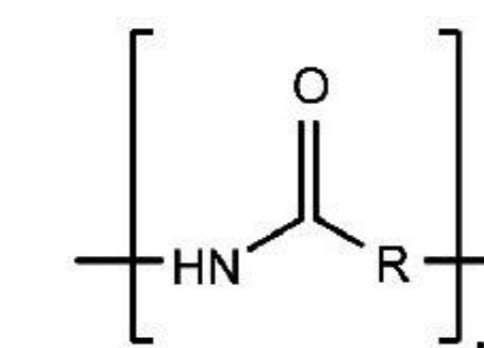
piceatannol

Increase in anticancer bioactivity

NANOTECHNOLOGY

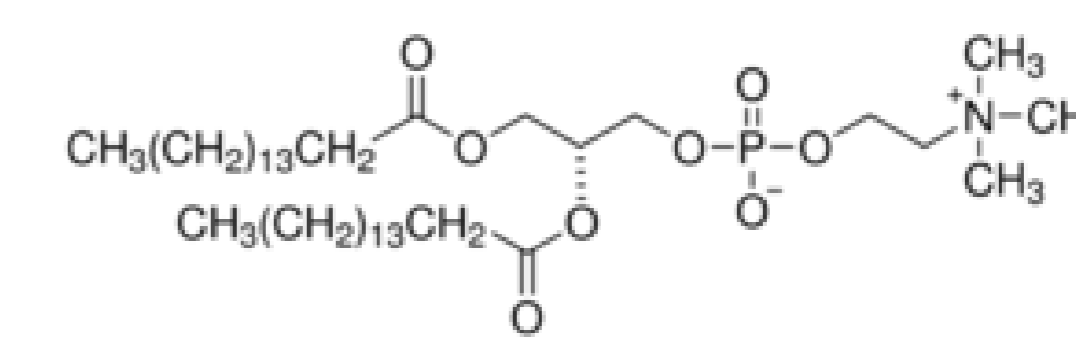


glyceryl monooleate liquid crystalline nanoparticles



Zein nanoparticles

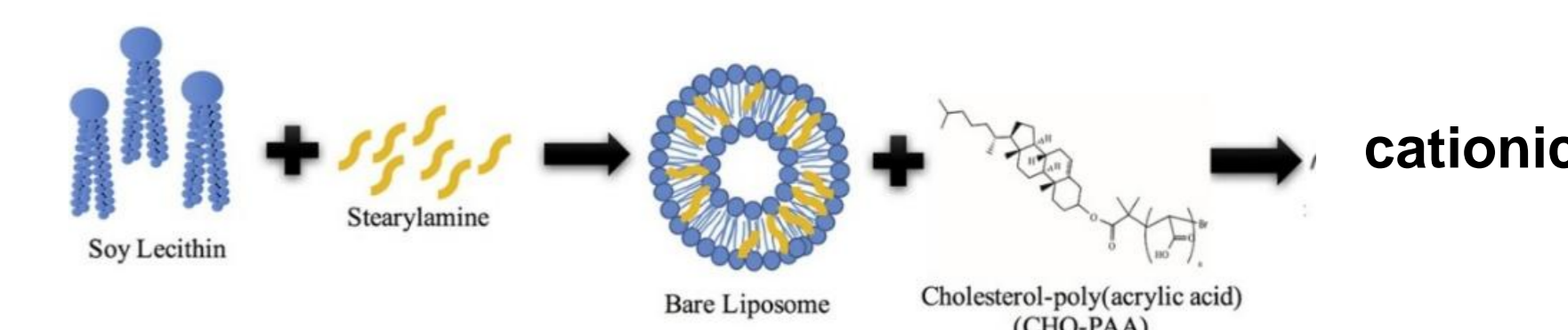
Nowadays nanotechnology-based RSV delivery systems which use various biocompatible materials, represent the most sophisticated method. Weather nutraceutical (biopolymer-based nanoparticles, emulsions) or parenteral (microbubbles, liposome) formulations, those delivery systems provide compelling alternatives for increasing RSV application potential and have the tenacity to evolve into widely applicable RSV carriers.



zwitterionic

(phosphatidyl-choline1, 2-dipalmitoyl-sn-glycero-3-phosphocholine)

Peanut oil, for example, is promising food-compatible way of RSV delivery but it seems that different liposomes: **zwitterionic** (made from saturated phosphatidyl-choline1, 2-dipalmitoyl-sn-glycero-3-phosphocholine and cholesterol) or **cationic** (made from soya lecithin, cholesterol and stearylamine) show precedence among other vehicles. RSV in cationic liposomes even have improved biological activity comparing to free RSV.



cationic