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Drug development Process

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LINAISMAIILL MAR 17, 2021 04:46PM

According to many studies and availabilty in Pharmacies, Most curcumins are prepared with black pepper. since black pepper enhances the permeabilty through the intestine wall and will slow the liver degredation. Hence, longer half life and more permeability.. This combination is essential to benefit from Curcumins.

Ali Awarke

Target identification
The pleiotropic effects of curcumin account for its ability to modulate and regulate diverse molecular targets. Curcumin embodies a unique chemical structure that potentiates direct or indirect binding with cellular target as well as upregulatory or downregulatory effects on certain transcription factors and gene products such as the interleukins (1-12), tumor necrosis factor (TNF) and interferon (INF)γ. This dynamic chemical architecture mediates multiple interactions such as extensive hydrogen bonding, covalent bonding, metal chelation and hydrophobic interactions with various molecular targets.
(Mira Al Achcar)

Lead identification / Characterization

Then next step is characterization of curcumin by using different methods as HPLC ,X ray diffraction to determine its crystalline structure, MS , UV/Visible
to determine its structure
(Fatima Awada)

Lead identification / Toxicity

Check for toxicity and mutaginicity by Ames test (A study said that CEC which is one of the commercial curcumin formulations was confirmed to be non mutagenic as it give significantly similar result to that of a negative control so it was not able to induce the growth of Salmonella typhimurium at the conditions done in the article)Fatima Awada

Lead optimization and product characterization

After target identification and validation and lead identification, we move on to lead optimization and characterization. Physicochemical studies (determining structure and physicochemical properties)..... are performed to get a general idea about the molecule's drugability and methods that can be applied to produce the optimal molecule structure and dosage form that could provide high bioavailability of the compound. In preformulation and development, solubility,/accelerated stability testing/solid state properties are evaluated for pharmaceutical formulation. In ADME, before absorption, a drug must undergo dissociation and dissolution in the aqueous medium of the GIT. To determine dissolution, we follow Lipinski's rule of 5.

Sama Zeaiter

Lead optimization

The bioavailibilty of curcumin can be enhanced by retarding its metabolism, increasing it's bioaccesibilty and promoting it's absorption..
The bioaccessibility of curcumin can be increased by enhancing the amount that is solubilized within the mixed micelles present in the small intestine. This may
be achieved by including surfactants, phospholipids, fatty acids, or monoglycerides within the
curcumin-loaded carrier particles, as these surface-active substances, can become incorporated into
the mixed micelles and increase their solubilization capacity.
In addition certains kind of food components including pipering in black pepper and some catechins in green tea, can inhibit efflux transporters, thereby increasing the amount of curcumin absorption by the body (hind chmayssem)

Lead Optimization

Before being absorbed, any drug formulation should be soluble in the stomach or intestine , where absorption occurs. And since curcumin has a low water solubility, surface acting agents should be added to render the solubility of this molecule in the stomach in order to be absorbed later on. Commonly used non-ionic surfactants are lauroyl macroglycerides, castor oil, di-fatty acid ester of low molecular weight polyethylene glycol...
Tiba

Lead optimization

1. **Nanoparticles Formulation**

In the second step of drug development before advancing to clinical research which is preclinical research, conveys formulation optimization and bioavailability. Curcumin is highly hydrophobic, rendering it unable to solvate in the intestinal fluid in order to be absorbed, which is solved through nanoparticles that permit to slowly transit in the gut which increase the local concentration gradient across the absorptive segments of intestine.

HMohsen

Lead Optimization: Increasing bioavailability of curcumarin through microemulsions

Increasing bioavailability of curcumarin through microemulsions through hydroxyl gels ,creams or microcapsule of gelatin to increase stability (yara haidar)

Lead optimization, high bioavailable form of curcumin and liposome technology

Since the curcumin gets metabolized before it can be absorbed, so we can increase its absorption in food or as designed drug. In food or as supplements we can mix it with piperene that inhibit its metabolism (enzyme inhibition) by stomach, intestine and liver and increase its bioavailability, or by heat to increase its solubility in water or mix it with healthy fat since it is fat soluble. Now to increase its bioavailability with a certain formulation as a designed drug we can mix it with liposome because they are considered as effective drug carriers so that they interact directly with cells more than the regular curcumin supplements.
Lama Zeaiter

Lead optimization

Generally, the oral bioavailability of curcumin is low due to a relatively low absorption by small intestine coupled to an extensive reductive and conjugative metabolism in the liver and an elimination through the gall bladder , that's why several strategies such as inhibition of curcumin metabolism with adjuvants as well as novel solid and liquid oral delivery systems have been tried to counteract curcumin poor absorption and rapid elimination from the body. Some of these drug deliveries can successfully enhance the solubility, extending the residence in plasma, improving the pharmacokinetic profile and the cellular uptake. Rawan Bitar

Lead Optimization/ Bioavailability

To increase the bioavailability of curcumin, we mix and consume this spice with a source of fat (nut butters...), or combining with a healthy oil (coconut oil...). By this way curcumin will directly be absorbed into the blood stream through the lymphatic system, bypassing the liver.
Another way is the use of delivery systems such as micelles, liposomes and microemulsions. They enhance efficacy by enhancing small intestine permeation and preventing degradation in the meduim.
Rania Barakat.

Enhancing curcumin effects

Many approaches can be applied to solve the issue: 1 1-first to increase its absorption and therefore bioavailability, from a dosage form point of view, this hydrophobic curcumin can be wraped in hydrophilic microspheres to increase their absorption ; or we can find some molecules that have synergistic effect ans increase its absorption ; also taking it with fatty meals
2- Another approach is : further studying curcumin to determine the essential structure to cause effect ,and then apply some modifications to the structure while maintaining its beneficial activity.
Rima Kamal

Lead Optimization - Enhancing Bioavailability of Curcumin

Enhancing the bioavailability of oral curcumin is done using different novel delivery systems:
1- Combination of curcumin and Piperine
2- Association of curcumin and lecithin
3- curcumin in hydrophilic Nano particules
4- curcumin in the lipid based formulations
5- curcumin in the micellar system
6- curcumin in chitosan nano particles
7- miscellaneous

Addition of some adjuvants in order to decrease the level of biotransformation and metabolism,and therefore extend the presence of the molecule in the body