

THE IMPRESSIVE RESPONSE OF HERBAL BIOACTIVES TOWARDS BIOAVAILABILITY

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Received 15th Jan. 2024; Revised 19th Feb. 2024; Accepted 8th July 2024; Available online 1st May 2025

<https://doi.org/10.31032/IJBPAS/2025/14.5.8986>

ABSTRACT

The poor bioavailability of several drugs have been a major problem therefore we need to increase the amount of dose in order to get desired bioavailability and that sometimes lead to drug toxicity. To increase the efficacy or bioavailability of drugs herbal bioenhancers are majorly preferred. The bioenhancers are the substance or adjuvants who increases the bioavailability of drug without showing their own therapeutic response, in regard to this herbal bioenhancers have shown the impressive response by enhancing the bioavailability through the chief mechanism of outlawing p-glycoprotein, outlawing CYP-450 enzyme or by enhancing the rate of absorption. Many herbal bioenhancer such as piperine, curcumin, niaziridin, etc have increased the bioavailability of drug.

Keywords: Bioenhancer, Herbal Bioenhancer, P-glycoprotein, CYP-450, Absorption

1. INTRODUCTION:

1.1. Herbal Bioenhancer:

Bioavailability refers to the proportion of a substance that enters the bloodstream when introduced into the body and is made available for the storage. In pharmacology, it refers to

the fraction of a drug that reaches the systemic circulation after administration and is thus able to produce its intended effects.

Bioavailability is one of the important parameter for any of the choice of drug. The drugs with better bioavailability show better therapeutic effect with minimum dose. Factors such as absorption, distribution, metabolism, and excretion play crucial roles in determining the bioavailability of substances in various contexts, including pharmaceuticals and nutrition [1, 2].

Maximum bioavailability is attained by drugs administered via intravenous route, whereas drug administered orally are poorly bioavailable as they readily undergo first pass metabolism and incomplete absorption, such unutilized drug in the body may lead to adverse effects and also drug resistance [3]. Thus, there is need of molecules which themselves have no same therapeutic activity but when combined with other drugs or molecules enhance the their bioavailability. The bioavailability or adjuvant, is a substance that improves the absorption and bioavailability of another compound without any pharmacological activity of its own therapeutic dose used.

Herbal bioenhancers are natural substances, often derived from plants, that enhance the bioavailability and efficacy of various compounds, including nutrients and drugs. They interact with metabolic processes, improving absorption or utilization in the

body [3]. Currently herbal bioenhancers are used to improve the absorption and ultimately the bioavailability of the various drugs activities used to treat disease and disorder associated with central nervous system CNS, gastrointestinal tract, and cardiovascular system [4].

1.2. Need for Bioenhancer:

The biological membrane present in our body are lipophilic in nature i.e, they are lipid soluble. There are several drugs having excellence bioactivity in vitro demonstration but no in-vivo show less or no actions due to their poor lipid solubility [5].

Molecular size are also one of the major limiting factor for molecules to pass through the biological membrane resulting poor absorption and poor bioavailability, due to the low lipid solubility and large molecular size the drugs administered are required in high dose which later can show adverse effect and there can also be the chances of contraindication of drug which can be threatening for the patient's life.

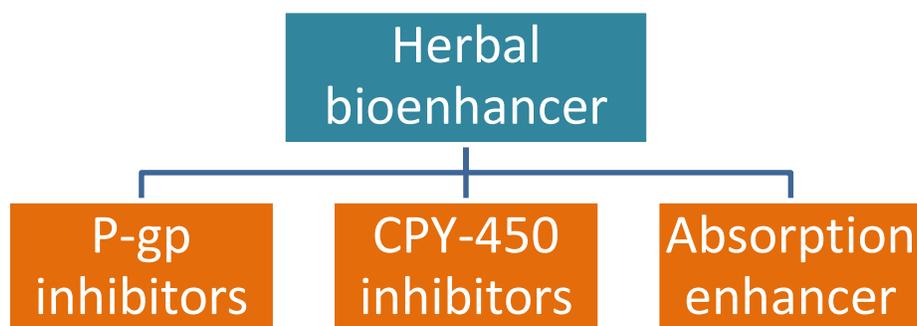
1.3. Mechanism of Bioenhancers:

The bioenhancer work by increasing the bioavailability of various drugs through showing chief mechanism such as-

- Enhancing the time of absorption of orally administered drugs

- It reduces the secretion hydrochloric acid from stomach
- It also decreases the process of metabolism and excretion for extending the stay of drug in the body by various ways.

The herbal bioenhancers improve the bioavailability of various drugs molecules majorly by outlawing P-glycoprotein efflux, outlawing of cytochrome P-450 and enhancing the rate of absorption [5].



- **Outlawing of p-glycoprotein**

p-gp regulates the intracellular uptake and distribution of xenobiotics and toxins in the body [6]. This p-gp also limits the permeability and absorption of various drugs through the efflux mechanism, which ultimately results in low concentration of drug in the cells. so, to have optimum bioavailability and efficient drug delivery it is important to inhibit the action of p-gp, that is done by the herbal bioenhancers which ultimately result in the increase in the time duration of drug in the body. Hence, bioavailability increases.

- **Outlawing of Cytochrome-P450**

The enzymes of cytochrome-P450 family are largely responsible for the first pass metabolism and elimination of multiple drugs [7]. To increase the bioavailability of drugs which undergo first pass metabolism by cyp-450, it is important to inhibit the action of cyp enzyme. The herbal bioenhancers suppresses the action of cyp-450 enzymes to decrease the amount of drugs undergoing first pass metabolism and their excretion.

- **Absorption penetration**

BCS classification of many drugs is influenced by Membrane permeability [7]. The improper or inadequate permeability of certain drugs significantly decrease the absorption of the drug and their therapeutic

effect. Alteration in the permeability of these drugs can trigger their absorption optimally [7].

This enhancement mechanism of permeability can be achieved with the use of many herbal

bioenhancers such as, Niaziridine, Gingerol, Aelovera etc. [6]. The drug molecules permeation increases through the biological membranes, thus giving better and improved absorption and bioavailability.

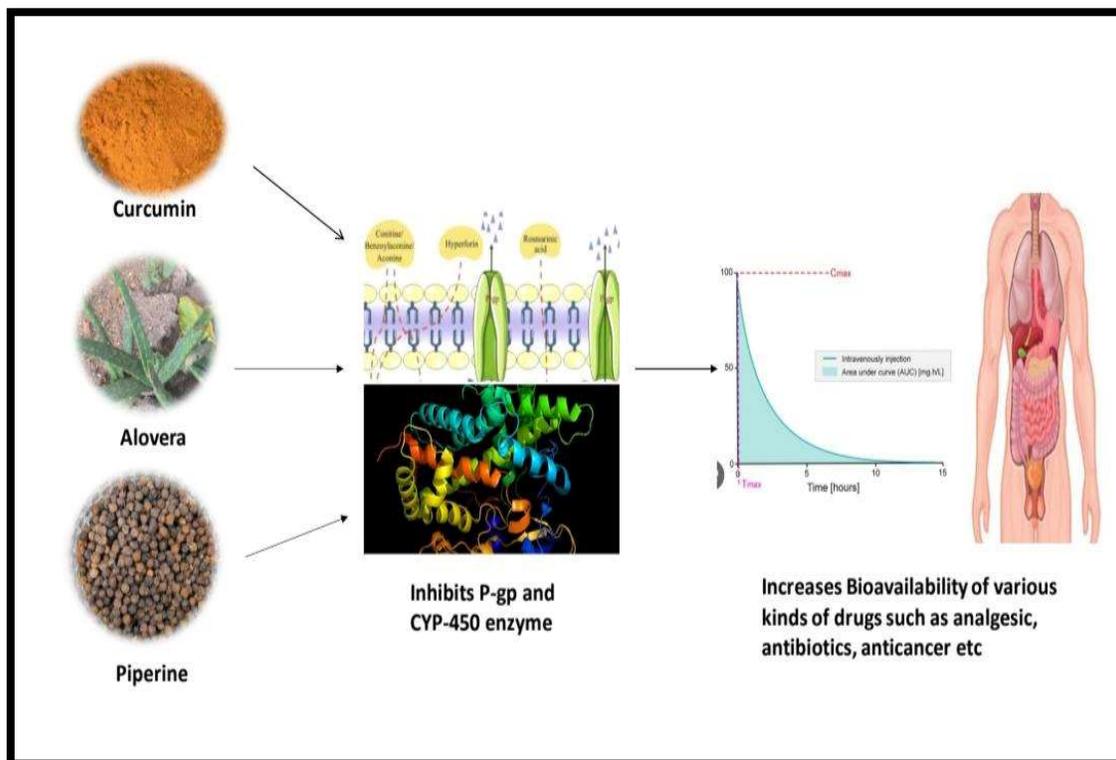


Figure 1: Effect of Herbal Bioenhancer

1.4.Uses:

Herbal bioenhancer, also known as bioavailability enhancers or adjuvants, are the substances derived from plants that can improve the absorption and efficacy of other compounds, particularly pharmaceutical drugs or nutrients. Some common uses include

- Enhancing drug absorption: herbal bioenhancer can improve the absorption of drugs, allowing for lower doses to be

effective or reducing the risk of side effects [8].

- Improving nutrient absorption:- they can increase the absorption of essential nutrients such as vitamins, minerals and amino acids, promoting better overall health.
- Potentiating herbal remedies:- herbal bioenhancers are often used to enhance the effectiveness of herbal remedies or

supplement, making them more potent and efficient.

- Supporting digestion:- some herbal bioenhancers can support digestion and nutrient absorption by improving gastrointestinal functions, which can be beneficial for individuals with digestive issues.
- Combating drug resistance:- in some cases, herbal bioenhancer have been investigated for their potential to overcome drug resistance in certain diseases by improving the bioavailability of medication [8].

Overall, herbal bioenhancers have diverse application in improving the effectiveness of various components and promoting better health outcomes. However, its essential to use them under the guidance of healthcare professional to ensure safety and efficacy.

1.5. Examples:

1.5.1. Piperine

Piperine is one of the renowned bioenhancer known for inhibiting P-glycoprotein. The piperine is the major alkaloid fruit chemically [1, 5- (1, 3 Benzodioxol-5-yl)-1-oxo, 2, 4-pentadienyl] obtained from *Piper nigrum* L. (Black pepper) belonging to the family Piperaceae [9]. The bioavailability of many classes of drugs such as the drugs used for cardiovascular system, non-steroidal

anti-inflammatory drugs, antibiotics, antituberculosis etc. have been induced by the use of piperine [7]. It enhances the bioavailability of structurally and therapeutically different drugs, either by increasing the absorption or by delaying the metabolism of the drug or by a combination of the both processes. Piperine has been used as bio-enhancer for a number of drugs in allopathic system of medicine like oxyphenbutazone, phenytoin, aflatoxin B1, beta-carotene, propranolol and theophylline [10]. It promotes the rapid absorption from gastro-intestinal tract or by protecting the drug molecule from being metabolized in its first pass metabolism through the liver by the CYP 450 enzyme. The molecular formula of piperidine is C₁₇H₁₉O₃N. Its pH is 8.6- 8.5 and pKa is 13.2 [10]. Piperine may also interact with the process of oxidative phosphorylation process like activation/deactivation of certain metabolic pathways, slowing down the metabolism and biodegradation of drugs [5]. This action of piperine results in higher plasma levels of the drugs, rendering them more available for pharmacological action. Piperine has been used as bioenhancer for certain antibacterial-antibiotics with promising results. The interaction of piperine with drug-metabolizing enzymes is responsible for oxidation,

hydroxylation and glucuronidation. Piperine appears to top in the list of bioenhancers as it has been used as bioenhancer for Allopathic, Ayurvedic and unani drugs

Some key points about piperine as a herbal bioenhancer include:

Enhanced Nutrient Absorption: Piperine can increase the absorption of nutrients such as vitamins (e.g., vitamin C, vitamin B6), minerals (e.g., selenium, iron), and phytochemicals (e.g., curcumin, resveratrol) by inhibiting enzymes responsible for their metabolism.

Improved Drug Bioavailability: Piperine has been studied for its ability to enhance the bioavailability of various drugs, including antibiotics, analgesics, and anti-cancer drugs. By inhibiting drug-metabolizing enzymes, piperine can increase the concentration of drugs in the bloodstream, potentially improving their efficacy [11].

Potential Health Benefits: piperine have several health benefits, including antioxidant, anti-inflammatory, anti-cancer, and antidepressant effects. These effects are attributed to its ability to modulate various molecular pathways in the body.

Safety Considerations: While piperine is generally regarded as safe when consumed in small amounts as a spice or food additive, high doses may have adverse effects, including

gastrointestinal irritation and interactions with certain medications. It's important to consult with a healthcare professional before using piperine supplements, especially if you are taking medications or have underlying health concern [12].

1.5.2. Curcumin:

curcumin is a compound found in turmeric. Curcumin is a bioenhancer which enhances the bioavailability and absorption of various drugs and xenobiotics. It is often used in combination with other substances to enhance their absorption and therapeutic effects [13]. The effects of curcumin bioenhancer include improved absorption and bioavailability of co-administered substances. It can enhance the therapeutic effects of drugs and supplements by increasing their concentration in the bloodstream and target tissues. Additionally, curcumin itself exhibits various health effects, including anti-inflammatory, antioxidant, antimicrobial, and anticancer activities.

the efficacy of curcumin depends on various factors, including dosage, formulation, and individual differences in metabolism [14]. Curcumin acts as a bioenhancer by inhibiting drug-metabolizing enzymes and increasing the absorption of other compounds. It primarily achieves this by inhibiting enzymes like cytochrome P450 and P-glycoprotein,

which are involved in drug metabolism and efflux transport, respectively.

1.5.3. AloeVera:

Aloe vera has been recognized for its numerous health benefits for long, Aloe vera, a succulent plant known for its therapeutic properties, has emerged as a promising bioenhancer in recent years. Aloe vera contains polysaccharides and mucilaginous compounds that form a gel-like substance in the gastrointestinal tract. This gel can increase the absorption of nutrients and drugs by slowing down their transit through the digestive system, allowing for better uptake [10].

Aloe vera, leaves, contains a rich array of bioactive components that possess bioenhancing properties. By harnessing the bioenhancing potential of aloe vera, it is possible to enhance the absorption and bioavailability of drugs and bioactive compounds [15]. This can lead to improved therapeutic outcomes, reduced dosage requirements, and minimized side effects. Aloe vera has been found to modulate drug-metabolizing enzymes, such as cytochrome P450 enzymes, in the liver and intestine Aloe vera contains various enzymes, such as amylase, lipase, and alkaline phosphatase, which can modulate the activity of other enzymes involved in drug metabolism. This

modulation can affect the bioavailability and efficacy of certain medications. It can inhibit or induce specific enzymes involved in drug metabolism, leading to altered pharmacokinetics of co-administered drugs. This modulation can result in enhanced drug concentration, prolonged half-life, and improved therapeutic outcomes [15]. Additionally, aloe vera has anti-inflammatory, antioxidant, and immunomodulatory properties, which further contribute to its bioenhancing effects. However, it's important to note that more research is needed to fully understand the mechanisms and potential interactions of aloe vera as a bioenhancer.:

Enzyme Modulation:

Gut Microbiota Interaction: Aloe vera may interact with the gut microbiota, influencing their composition and metabolic activity. This interaction can affect the metabolism and bioavailability of drugs and nutrients.

Uses of aloe vera as a herbal bioenhancer include:

- **Nutrient Absorption:** Aloe vera can enhance the absorption of nutrients such as vitamins, minerals, and antioxidants, potentially improving overall nutritional status.
- **Drug Delivery:** Aloe vera may be used to improve the bioavailability and effectiveness of certain drugs,

reducing the required dosage and minimizing side effects.

- Health Supplements: Aloe vera supplements or extracts may be used in combination with other nutrients or medications to enhance their therapeutic effects.

Effects of aloe vera as a herbal bioenhancer may include:

Improved Nutrient Utilization: By enhancing nutrient absorption, aloe vera can support overall health and well-being.

Enhanced Drug Efficacy: Aloe vera may improve the effectiveness of certain medications, leading to better treatment outcomes.

Potential Side Effects: While aloe vera is generally considered safe when used topically or orally in moderate amounts, excessive consumption may lead to gastrointestinal discomfort or allergic reactions in some individuals.

It's essential to consult with a healthcare professional before using aloe vera or any other herbal supplement, especially if you're taking medications or have underlying health conditions.

2. CONCLUSION:

There are various drugs which have been used to treat or prevent the various types of disease but the problems occur with the several drugs

are their poor bioavailability. They generally get metabolized by CYP-450 enzyme, or effluxed by p-glycoprotein in GIT or have poor absorption. Several herbal bioenhancers such as piperine, curcumin, stevia, aloe vera have been used to increase the bioavailability of drug by increasing the absorption or by delaying the metabolism of the drug or by combination of both. Hence, we come to an end that the use of herbal bioenhancers along with reduces a drug toxicity and increases the bioavailability.

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