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Herbal Bioenhancers: Nature's Gift to Improve Drug Efficacy – A Review

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ABSTRACT

The use of bio-enhancers has gained attention in recent times due, to their ability to enhance the effectiveness and bioavailability of orally administered medications. The concept of bioenhancers. Emphasize their significance in overcoming hurdles related to drug absorption. The history, definition, role, ideal properties, advantages and diverse applications of bioenhancers are discussed to provide insights. Additionally, we explore the criteria for selecting active ingredients as a foundation for an exploration of these naturally occurring compounds. Classification of bioenhancers offers an overview of these biologically active substances. Mechanisms through which bioenhancers improve drug absorption, provides an understanding of how they function within the body. Examples of bioenhancers that highlight their various sources and their ability to enhance the potency of drugs. Formulations derived from parts of plants to showcase the diverse range of bioenhancers found in nature. Prospects of bioenhancers suggesting potential innovations and areas for further research. Conclusion is there for summarizing key takeaways. Emphasizing how herbal bioenhancers significantly contribute to advancing drug delivery and efficacy.

INTRODUCTION

Today, there's a medical need and interest to improve the bioavailability and efficacy of medicines for better therapeutic effects, especially when they are expensive or risky and need to be taken for a long period. Sometimes, these medicines don't work well because they can't be properly absorbed in our body, and patient might have to take very high doses or frequent doses that can cause side effects or toxicity. Various factors can make a medicine hard to absorb, like inadequate dissolution, poor solubility, or a fast metabolism.

So, there is a need for substances that can make these medicines work better when taken with them. Scientists and healthcare experts are always looking for ways to get the most out of drugs. This search has led them to an interesting area called "bioavailability enhancement". Substances that can increase bioavailability are called "bioenhancers". They don't have a synergistic effect with the medicines, but they help the medicines get into our bodies better without directly reacting with them [1], which means they are substances that don't have a therapeutic effect but enhance the absorption and biological activity of other substances when given in combination [2]. Bioenhancers are an ancient concept in Ayurveda. In Sanskrit, it is called "Yogvahi" (to rise in effect) [3]. Bioenhancers are one type of natural helper or booster that can make drugs or nutrients work even better. These natural helpers have sparked the interest of researchers and healthcare professionals, opening up new possibilities for improving the therapeutic effects of medicines, traditional healing methods, and nutritional supplements. The benefits of adding bio-enhancers include:

- reduced drug dose
- reduced cost of the drug
- reduced incidence of drug resistance
- reduced risk of side effects
- efficacy is enhanced by increased bioavailability
- reduced requirement of raw materials for drug manufacture

For instance, this is especially beneficial in anticancer drugs like Taxol, used to treat breast cancer. This drug is obtained from the Yew tree, one of the slowest growing trees in the

world, and to obtain Taxol for one patient, six trees of 25-100 years need to be chopped. Simply adding a bioenhancer to Taxol means that fewer trees need to be sacrificed [4]. By using bioenhancers into modern medicine, it will not only make treatments work better, but it will also be following the trend of personalized healthcare and using sustainable, plant-based remedies, which is cheaper and have less side effects. In a time when people looking for ways to be healthier and happier, bioenhancers are a bridge between the old and the new, offering amazing possibilities for the future of healthcare and well-being.

Concept & History of Bioenhancers:

The concept of 'bioavailability enhancers' is derived from the traditional, age-old system of Ayurveda (the science of life). In Ayurveda, black pepper (Piper nigrum), long pepper (Piper longum), and ginger (Zingiber officinale) are collectively known as "TRIKATU". In Sanskrit, Trikatu means three cards.

The action of enhancers was first documented by Bose in 1929, who described the action of long pepper on Adhatoda Vasika leaves as increasing the anti-asthmatic properties of Adhatoda Vasika leaves.

The term "bioavailability enhancers" was coined by C.K. Atal, the chairman of the Regional Research Laboratory in Jammu (now known as Indian Institute of Integrative Medicine, Jammu), when piperine was discovered as the world's first bioavailability enhancer in 1979. C.K. Atal examined a list of an ancient Indian Ayurvedic Formulations used in the treatment of a wide range of diseases. He observed that a majority of Ayurvedic formulations contained either Trikatu or else one of the ingredients of Trikatu, namely Piper longum used in a large variety of diseases. Based on this hypothesis, these ingredients were studied, which found that one of the ingredients, 'Piper longum', increased the bioavailability of many drugs. Piperine, the active principle present in Piper longum was isolated and its bioavailability enhancing action was established with the help of sparteine and vasicine. The RRL (Jammu) confirmed piperine as the world's first bioenhancer, which led to the creation of the world's first experimentally enhanced medicines.

Further research on several classes of drugs including antitubercular, leprosy, antibiotics, NSAIDS, CVS, and CNS drugs showed similar results. Piperine was found to increase the bioavailability of different drugs ranging from 30-200%. Subsequent research has shown that it increases curcumin bioavailability by almost tenfold. However, it was also noted that

piperine did not increase bioavailability of all drugs, while with some drugs the effect was found to be inconsistent.

Significant data was published by RRL in various national and international journals and patent were filed in India, Europe, and USA. The first bioenhanced anti-tubercular drug, named as "Risorine" was launched in 2009 as Public-Private Partnership (PPP) between Indian Institute of Integrative Medicine (IIIM), Council of Scientific and Industrial Research (CSIR), and Cadila Pharma Ltd. Risorine contained 200 mg of Rifampicin, 300 mg of Isoniazid and 10 mg of Piperine. In 2011, on the occasion of World Tuberculosis Day, Risorine was issued as first bioenhanced anti-tubercular drug by Drug Controller General of India (DCGI) and presented to Mr. Bill Gates (Chairman of Microsoft).

Piperine increases bioavailability of rifampicin by about 60% and also reduces the dose of rifampicin from 450 mg to 200 mg. This reduces dosage, cost and toxicity of rifampicin. The discovery of piperine opened up new possibilities in the field of medical science and led to the discovery of many other enhancers. Piperine remains the most potent and extensively studied bioenhancer, known for its safety, effectiveness, affordability and versatility in enhancing various drug classes [5-8].

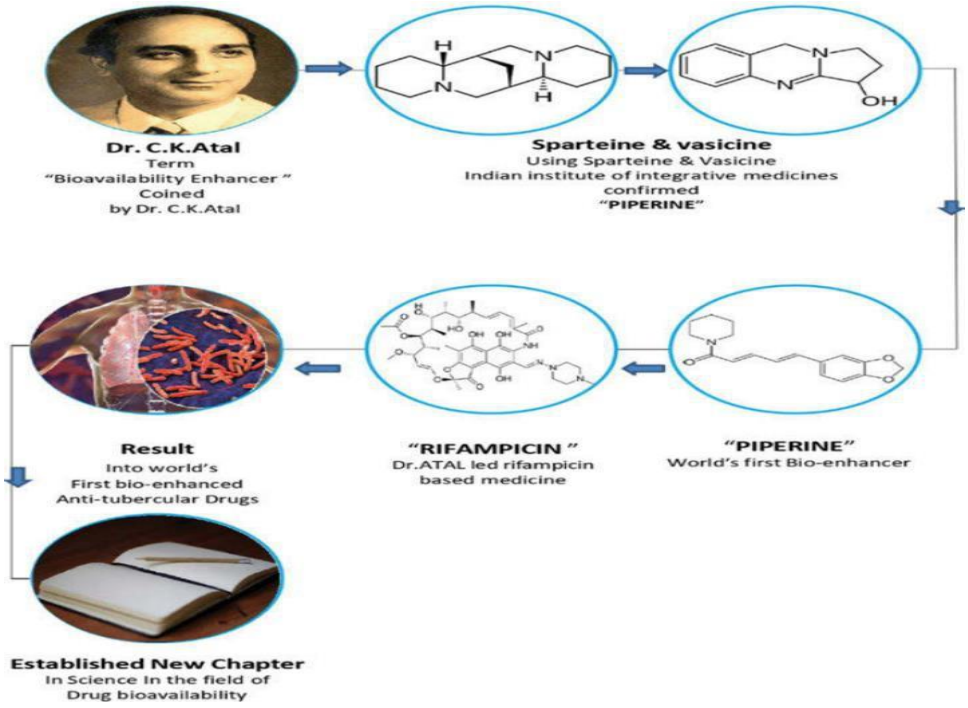

Fig (1): Pictorial representation of history of bioenhancers

Bioavailability and Bio-efficacy Enhancing Activity:

Bioavailability is defined as the extent and rate to which the active drug ingredient or active moiety from the drug product is absorbed and becomes available at the site of drug action. The term bioavailability and bio-efficacy enhancing activity described as "a substance at a lower dosage and in combination with a drug or nutrient provides more availability of the drug by reducing the consumption of the drug or nutrient resulting in enhanced efficacy of the drugs". The great interest for the improvement of the bioavailability of a large number of drugs is because of their,

• Poor bioavailability

• Administration for long period of time

• Toxicity

• Cost

Various concerns are related to poor bioavailability of drugs. Poorly bioavailable drugs remain sub-therapeutic because a major portion of a dose never reaches the plasma or exerts its pharmaceutical effect unless and until very large doses are given, which may lead to serious side effects. Inter-subject variability is also a concern for a drug with a narrow safety margin. Incomplete oral bioavailability includes poor dissolution or low aqueous solubility, poor intestinal membrane permeation, degradation of the drug in gastric or intestinal fluids, and pre-systemic intestinal or hepatic metabolism. Many treatments are also accompanied by loss of essential nutraceuticals in the course of therapy. Many herbal drugs and extracts, in spite of their good in-vitro results, have shown less or negligible in-vivo activity, due to their poor lipid solubility or improper molecular size, resulting in poor absorption and therefore poor bioavailability.

Maximizing bioavailability is therapeutically important because the extent of bioavailability directly influences plasma concentrations and consequently therapeutic efficacy. Bioavailability enhancement can make the expensive drugs affordable and reduce the toxic effects by reducing the required dose of drugs.

Nowadays, with the development of technology, novel drug delivery system has opened the doors towards the elevation of enhancing the bioavailability of drugs. The last decade has witnessed many novel carriers such as liposomes, microspheres, nanoparticles,

transferosomes, ethosomes and lipid-based systems for successful modified delivery of various drugs [9,10].

Barriers to Drug Absorption:

The drug must cross the epithelial barrier of the intestinal mucosa, for it to be transported from the lumen of the gut into the systemic circulation and exerts its biological actions. There are many structures in the intestinal epithelium which serve as barriers to the transfer of drug from the gastrointestinal tract to the systemic circulation.

An aqueous stagnant layer due to its hydrophilic nature is potential barrier to the absorption of drugs. The membrane around layers are lipid bilayers containing proteins such as receptor and carrier molecules. Drugs cross the lipid membrane by passive diffusion or carrier-mediated transport which involves the spending of energy.

For the passage of small water-soluble molecules such as ethanol there are aqueous channels within the proteins. The drug molecules larger than about 0.4 nm face difficulty in passing through these aqueous channels.

Drug efflux pumps like PGP possess very important role in inhibiting efficient drug entry into the systemic circulation. PGP is a type of ATPase and an energy dependent transmembrane drug efflux pump, that belongs to members of ABC transporters. It has molecular weight of 170KDa and has 1280 amino acid residues. Since PGP is gaining importance in absorption enhancement much work has still been made about its modulation due to its substrate selectivity and distribution at the site of drug absorption [11].

Methods for Enhancement of Absorption of Orally Administered Drugs [12]:

There are various approaches in use to enhance the intestinal absorption of poorly absorbed drugs. These approaches are as follows:

1) Addition of Absorption Enhancers

2) Making of Prodrug

3) Formation of various dosage forms and different pharmaceutical approaches

4) With the action of PGP Inhibitors

1) Addition of Absorption Enhancers

Many of the absorption enhancers are effective in improving intestinal absorption, such as bile salts, surfactants, fatty acids, chelating agents, salicylates, and polymers. Chitosan, particularly trimethylated chitosan, increases drug absorption via paracellular route by redistribution of the cytoskeletal F-actin, causing the opening of the tight junctions. Bile, bile salts and fatty acids are the surfactants which acts as absorption enhancers by increases the solubility of hydrophobic drugs in the aqueous layer or by increasing the fluidity of the apical and basolateral membranes. Calcium chelators such as EGTA and EDTA enhance absorption by reducing the extracellular calcium concentration, leading to the disruption of cell-cell contacts.

2) Making of Prodrug

To enhance drug absorption and bioavailability, chemical modification of drugs to produce prodrug and more permeable analogues has been widely studied as a useful approach. Various ampicillin derivatives are one of the well-known examples of increasing the lipophilicity of agents to enhance absorption of a polar dug by prodrug strategy. Ampicillin due to its hydrophilic nature is only 30-40% absorbed from gastrointestinal tract. By esterification of carboxyl group of ampicillins, the prodrugs of ampicillin such as pivampicillin, bacampicillin and talampicillin were synthesized. These prodrugs were more lipophilic than the parent compound following oral administration and they showed higher bioavailability in comparison with ampicillin.

3) Formation of Various Dosage Forms and Different Pharmaceutical Approaches

Utilization of permeability-enhancing dosage forms is one of the most practical approaches to improve the intestinal absorption of poorly absorbed drugs. Various dosage formulations such as liposomes and emulsions enhanced the intestinal absorption of insoluble drugs. Particle size reduction such as micronization, nanoparticular carriers, complexation and liquid crystalline phases also maximize drug absorption.

4) With the Action of PGP Inhibitors

The application of PGP inhibitors in improving peroral drug delivery has gained special interest. Several studies to enhance oral bioavailability have demonstrated the possible use of PGP inhibitors that reverse PGP-mediated efflux in an attempt to improve the efficiency of drug transport across the epithelia. PGP inhibitors influence metabolism, absorption,

distribution, and elimination of PGP substrates in the process of modulating pharmacokinetics.

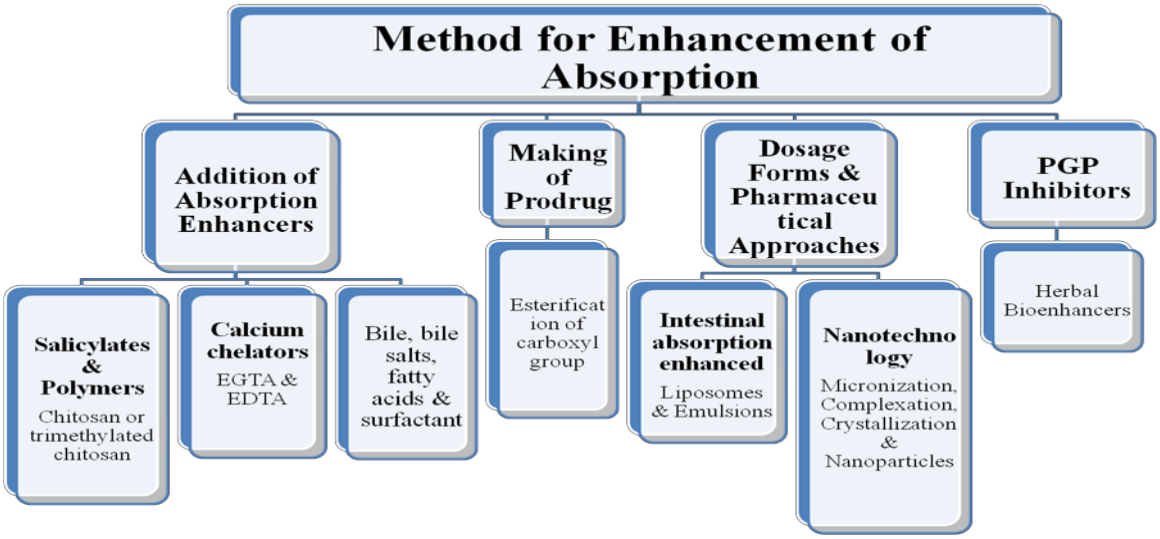

Fig. (2): Various Methods for Absorption Enhancement

What are bio-enhancers?

"Bioenhancers are substances from natural origin, which do not have their own therapeutic activity at the dose use. When it is combined with drug it increases bioavailability and bio-efficacy of specified drugs and leads to potentiation of pharmacological activity of that drug without synergistic effect [13]."

The bioenhancers are also called as "biopotentiators" and the phenomenon of bioavailability enhancement is known as "biopotentiation". There are two concepts related to Bioenhancers:

1) Anupaan**:** in which yogvahi is given with the food to increase its effect.

E.g. Amritdhara drops, used in GI diseases, by putting drops over sugar to increase potency.

2) Sehpaan**:** in which vehicle is used in the manufacturing of medicament.

E.g. Brahmi ghrita and panchgavyaghrit [14].

Role of Bioenhancers:

As the bioavailability increases, amount of drug required is decreases. Hence, the dose and price of medicines are often reduced, which makes the formulation cost-effective, safer, better tolerated, more efficient, better compliant, and having less drug resistance development [14].

Ideal Properties of Bioenhancers:

Various bio-enhancers have different properties, but they have some unique properties which is must require for their bio-enhancing ability and these ideal properties are as follows:

(1) It should be non-toxic, non-allergic, non-irritating to humans or animals.

(2) It should reduce side effects.

(3) It should reduce drug resistance.

(4) It should improve tolerability.

(6) It should be effective at a very low concentration in a combination.

(7) It should be easy to formulate into a various dosage form.

(8) It should enhance uptake or absorption.

(9) It should enhance activity of drug molecules.

(10) It should easily available and cost effective [15-18].

Advantages of bio-enhancers:

There are various advantages of using bioenhancer in combination therapy. These are as follows.

• Efficacy of drug is increase due to increase in bioavailability.

• Combination of bioenhancer with drug reduces the dosage and dangers of drug resistance can be minimized.

• Adverse drug reaction/side effects and toxicity of drug will be minimized because of reduced dosage. This is especially true of anticancer drugs like Taxol.

• There are ecological benefits too e.g. Taxol used to treat ovarian cancer or breast cancer is derived from dark of Pacific yew tree, one of the slowest growing trees in the world. At present to treat one patient, six trees, 25-100 years old need to be felled, but with bioenhancers fewer trees will be destroyed [19].

Application of Bioenhancers:

• Bioenhancers not only increase the availability of drugs in the body it also reduces the dose of drug because the good bioavailability decreases the dose of drug which is going to administered.

• It also prevents from the drug resistance and toxicity of antibiotics.

• These techniques of bio enhancers principally target to the toxic drugs, expensive drugs, rare drugs, poorly bio-available drugs and the drugs which are used for longer duration.

• However, it can also be used in any drugs influenced by bio-enhancers.

• The innovation and explanation of bioavailability enhancers has led to several patent applications.

• Piperine is marketed as mono-preparation bioenhancers and as a constituent of nutrition additive that contain different vitamins, curcumin, resveratrol or coenzymes.

• Bioenhancers can reduce the dosage and cost of expensive medication while making treatment safer, in humans first time its application has been done in treating TB for which the existing drugs are toxic and expensive and they are administered for longer periods. The drug risorine is approved against TB [20].

Classification of Bioenhancers [21-23]**:**

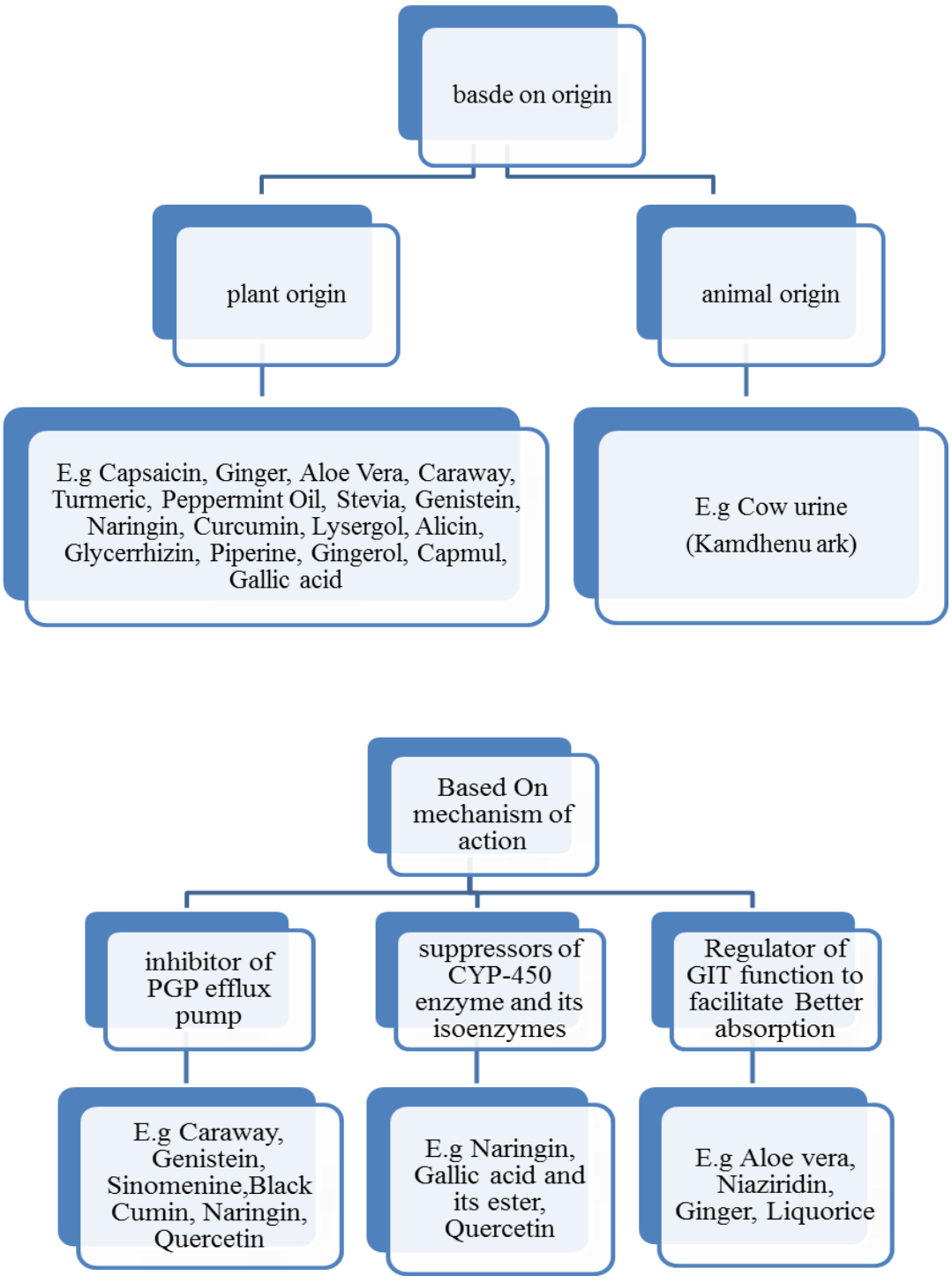

Fig (3): Classification of Bioenhancers

Mechanism of Action of Bioenhancers [24-34]:

Bio enhancer have various mechanisms of action and different bioenhancers shows same or different action.

1. by promoting absorption of drug from GIT by reducing HCL secretion and increasing blood supply.

2. Increasing the stay of what we eat in the GIT so that it has more time to get absorbed. By decreasing the intestinal motility and enhancing the time of stomach emptying.

3. By enhancing permeability of GIT epithelial cell membrane. Examples include niaziridin, piperine, gingerol etc.

4. It inhibits or reduces the rate of biotransformation of drug in the liver or intestine.

5. By modifying immune system to reduce overall requirement of drug.

6. By allowing entry into pathogen or by increasing penetration where they become persistors within microphases such as for mycobacterium tuberculosis. Example: nitrile glycosides.

7. By inhibiting ability of pathogen or tissue to reject the drug.

8. By hindering drug metabolizing enzymes like CYP3A4, CYP1A1, CYP1B2, CYP2E1 in lungs or various locations. Example: quercetin, naringin.

9. By stimulating gamma glutamyl transpeptidase (GGT) actively which enhances amino acid uptake.

10. By modifying signaling process between host and pathogen to increase accessibility of drug to pathogen.

11. By enhancing binding of drug to receptors, proteins, DNA, RNA and potentiate and prolong its effect.

12. Cholagogous effect i.e. it stimulates gall bladder contraction to promote flow.

13. By restraining renal clearance by preventing glomerular filtration and active tubular secretion by inhibiting P- glycoprotein and facilitating passive tubular reabsorption.

Examples of Bioenhancers [35-50]**:**

1) Piperine

■ **Biological Source:**

Piperine is an alkaloid obtained from the plant Piper longum (Long pepper) and

Piper nigrum (Black pepper).

■ **Family:** piperaceae.

■ **Dose:**

The bioenhancing dose of piperine is approximately 15mg/person/day and not more than 20mg/day in divided doses, which corresponds to from several thousand to up to 40,000 times less than the LD50 dose of piperine, as established in various experiments on rodents. The effective bioenhancing dose of piperine for drug compounds varies, but a dose of approximately 10% (w/w) of the active drug could be regarded as an appropriate bioenhancing dose for most drugs.

■ **Mechanism:**

Different mechanisms for the bioenhancer activity of Piperine have been proposed including DNA receptor binding, modulation of cell signal transduction and inhibition of drug effluent pump. In general, it

• inhibits drug-metabolizing enzyme,

• stimulates absorption, by stimulating gut amino acid transporters,

• inhibits the cell pump responsible for drug elimination from cells and.

• inhibits intestinal production of glucuronic acid, thus permitting a more active form of drug to enter the body.

It may increase the absorption of drugs in the GIT or inhibit enzymes responsible for drug metabolism, especially in the liver when the drug passes through the liver after absorption from GIT. Oral administration of Piperine in rats has strongly inhibited the hepatic arylhydrocarbon hydroxylase (AHH) and UDP- glucuronyltransferase activities.

Some of the metabolizing enzymes inhibited or induced by Piperine include. CYP1A1, CYP1B1, CYP1B2, CYP2E1, CYP2A4.

■ **Drugs with Bioenhancer:**

Diclofenac sodium, pentazocin, phenobarbitone, propranolol, theophylline, metronidazole, methotrexate, etoposide, 18-ß glycyrrhetic acid, nateglinide, ibuprofen, resveratrol, fexofenadine, carbamazepine, nevirapine, phenytoin, etc.

2) Ginger

■ **Biological Source:**

Ginger is the dried underground stem or rhizome of the zingiberous, herbaceous plant Zingiber officials Linn, which constitutes one of the most important major spices of India.

■ **Family:** Zingiberaceae.

■ **Dose:**

The effective dose of the bioenhancer extract is in the range of 30 mg/kg body weight.

■ **Mechanism:**

The saponins, flavonoids, and alkaloids in ginger have a powerful effect on the GIT mucosa membrane. Ginger aids absorption by modulating gastrointestinal function.

■ **Drug with Bioenhancer:**

By use of ginger, the bioavailability of many antibiotics like Azithromycin (85%), Erythromycin (105%), Cephalexin (85%), Cefadroxil (65%), Amoxycillin (90%), and Cloxacillin (90%) are increased by using its constituents.

3) Curcumin

■ **Biological Source:**

Curcumin (diferuloylmethane) is the major curcuminoid contained in the rhizome of Curcuma longa Linn.

■ **Family:** Zingiberaceae.

■ **Dose:** The bioenhancing dose of curcumin is approximately 12gm/day.

■ **Mechanism:**

It suppresses drug-metabolizing enzyme like CYP3A4 in the liver as well as imparting changes in the drug transporter P – glycoprotein efflux pump inhibition. The bioenhancing nature of curcumin is similar to piperine. It suppresses UDP- glucuronyl transferase level in intestine and hepatic tissues. It also physiological activity in the gastrointestinal tract leading to greater absorption of drugs.

■ **Drug with Bioenhancer:**

Example of drug include norfloxacin, midazolam, celipropol, docetaxel, and methotrexate

4) Niaziridin (Moringa Oleifera)

■ **Biological Source:**

Niaziridin, a fresh nitrile glycoside, was isolated from the Moringa oleifera pods, leaves and barks.

■ **Family:** Moringaceae.

■ **Dose:** Niaziridin is used in the range between 0.1µg/mL to 10 µg/ml.

■ **Mechanism:**

The biomolecule enhances the absorption of drugs, vitamins and nutrients through the gastrointestinal membrane increasing their bioavailability. Therefore, Niaziridin can be used in combination therapy with drugs and nutrients resulting in reduced cost and duration of chemotherapy.

■ **Drug with Bioenhancer:**

These glycosides enhanced the absorption of commonly used antibiotics such as rifampicin, Tetracycline and ampicillin, vitamins, and nutrients.

5) Quercetin

■ **Biological Source:**

It is an aglycone form of several flavonoid glycosides found highest in onions.

■ **Family:** Liliaceae.

■ **Dose:** It enhances the bioavailability of Losartan at 10 mg/kg, Cefprozil at 500 mg/day, and Clopidogrel at 250 mg/kg.

■ **Mechanism:** It exhibits action by inhibiting CYP3A4 and PGP efflux pump.

■ **Drug with Bioenhancers:**

Quercetin is shown to increase the bioavailability, blood levels and efficacy of a number of drugs including Losartan, Cefprozil, Clopidogrel, Diltiazam.

Herbal Formulations Used as Bioenhancers Derived from Various Plant Part:

Various herbal formulations of bioenhancers are available. A well-known formulation is "Risorine". In November, 2009 Drug Control General of India (DCGI) approved Risorine as the first bioenhanced antitubercular formulation, which is prepared by Cadila Pharma Ltd. in partnership with Indian Institute of Integrative Medicine (IIIM) and Council of Scientific and Industrial Research (CSIR). Risorine contain 200 mg of Rifampicin, 300 mg of Isoniazid and 10 mg of Piperine. Piperine increases the bioavailability of rifampicin by 60% and reduce its dose from 450 mg to 200 mg.

Some other herbal formulations are as follows [51]:

1) Herbal Liposomal Formulation

2) Transferosome

3) Microsphere

4) Nanoparticles

5) Lipid Based Herbal Formulation

Table 1: Herbal Liposomal Formulation

Formulation	**Active Ingredient**	**Application**
Quercetin liposome	Quercetin	Lower dose, improved dispersion in BBB
Liposome encapsulated silymarin	Silymarin	get better bioavailability

Table 2: Transferosomes

Formulation	Active Ingredient	Application
Capsaicin Transferosomes	Capsaicin	Increase skin penetration
Colchicine transferosomes	Colchicine	Increase skin penetration

Table 3: Microspheres

Formulation	Active Ingredient	Application
Rutin alginate chitosan microspheres	Rutin	Targeting into cardiovascular & Cerebrovascular system
Zedoary oil microspheres	Zedoary	Sustained release and higher bioavailability

Table 4: Nanoparticles

Formulation	Active Ingredient	Application
Triptolide nanoparticles	Triptolide	Enhance the penetration of drug
Nanoparticle of cascade	chinensis Flavonoid and lignans	Improve water solubility

Table 5: Lipid Based Herbal Formulations

Formulation	Active Ingredient	Application
Ginkgo biloba lipid-based systems	Flavonoids	Stabilizes ROS
Silybin lipid-based systems	Flavonoids	Inhibit lipid peroxidation

Future Prospects of Herbal Bioenhancers:

The future outlook, for bioenhancers looks promising. As the demand for sustainable healthcare options continues to rise herbal bioenhancers, which are compounds derived from plants that enhance the effectiveness and availability of drugs or nutrients are expected to receive more attention. Here are some potential trends and opportunities;

1) Increased Research; Scientists are likely to conduct research to identify and validate bioenhancers exploring their potential benefits and how they work.

2) Nutraceuticals and Supplements; Herbal bioenhancers may gain popularity in the development of supplements and nutraceuticals aimed at improving the absorption of nutrients and compounds.

3) Integration into Traditional Medicine; Herbal bioenhancers have been used in medicine systems for centuries. They may become integrated into healthcare as alternative therapies.

4) Advancements in Drug Development; Pharmaceutical companies might explore the use of bioenhancers to enhance the effectiveness of drug formulations potentially reducing dosages and minimizing side effects.

5) Regulatory Frameworks; with increasing popularity, there may be a need for frameworks to ensure the safety and efficacy of herbal bioenhancer products.

6) Consumer Demand; the growing interest among consumers in holistic approaches to health is expected to drive the demand for bioenhancer products.

Overall these factors contribute to an outlook for bioenhancers, as a valuable part of future healthcare practices. It is worth mentioning that although herbal bioenhancers show promise in terms of benefits, it is essential to conduct research and rigorous testing to ensure their safety and effectiveness, in different applications. Furthermore, it is important to consider that people's reactions to these substances can differ which means personalized healthcare approaches may also be factors, in determining their usage.

Conclusion:

The research on bio-enhancers discussed in this review suggest that they have the potential to improve the absorption and effectiveness of various drugs and nutrients. These natural compounds, derived from plants with a history of use, show promise in helping the body make better use of medications.

As the healthcare industry explores complementary and alternative medicine, incorporating bio-enhancers could enhance treatment outcomes, potentially reducing the need for high drug doses and minimizing side effects. We hope this review encourages further research and exploration, leading to more effective and holistic treatment strategies.

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