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HERBAL BIO-ENHANCERS: AN INNOVATIVE CONCEPT IN CURRENT MEDICINE.

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ABSTRACT

The bioenhancers: Dr. Bose initially mentioned the idea in 1929. Indian scientists initially used the term "bioenhancers" in 1979 at the RRL in Jammu, now known as the Indian Institute of Integrative Medicine. The first bioenhancer, piperine was discovered in 1979. Following then, a lot of study was conducted in the area of bioenhancer development. A bioenhancer is a substance that, at the amount employed, can increase the bioavailability and bioefficacy of the medicine with which it is combined without exhibiting any usual pharmacological activity of its own. The cost of therapy has long been a key concern for poor nations. To make treatment more accessible to the general public, scientists have been working hard. Environmental modifications typically have a favorable effect on a nation's economy by reducing the cost of prescription medication and research. When a bioavailable medicine is taken in high doses, toxicity is decreased. In addition, it gets rid of drug resistance and cuts down on treatment time in half.

KEYWORDS: Bio-enhancers, Bio-availability, Bio-efficacy, P-glycoprotein.

INTRODUCTION

The discovery of piperine, the first bio-enhancer in the world, opened a new area of medical research known as bio-enhancers, bio-potentiators or bio-availability enhancers. It is a medical device that reduces the body's natural processes for degrading, discarding, and eliminating a variety of medications taken orally. Bio-enhancers are defined as substances that boost an active ingredient's bioavailability, leading to higher bioefficacy, without exhibiting any pharmacological activity of their own at the dosage used.[1] They may boost the bioavailability of toxins, vitamins, minerals, and allopathic medications, depending on their method of action. For instance, piperine increases the bioavailability of a number of nutrients and medications, including phenytoin, theophylline, and propranolol, as well as a toxin known as aflatoxin B1.[2]

HISTORY[3]

Bose was the first person to suggest the idea of bio-enhancers in 1929.[1] Before 1979, there was no such thing as a bio-enhancer or solubility enhancer as a word or chapter in any of the published works of science. Indian researchers first used the term "bio-availability enhancers" in 1979 at Jammu's Indian Institute of Integrative Medicine (Dr. C. K. Atal, the Director of

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institute RRL Jammu proposed the hypothesis of increased bio-availability of drugs from a clue during research on traditional medicinal drugs). The idea of bio-availability enhancers was then thoroughly studied and developed by him and his RRL Jammu research team. Utilizing Sparteine and Vasicine, the institution discovered Piperine as the first bio-enhancer in the world and scientifically demonstrated its effectiveness.

CLASSIFICATION[4,5]

Both the action location and the origin of a bio-enhancer—which may be either plant- or animal-based—are used to classify them. The availability of other molecules is increased by bio-enhancers, which are primarily found in plants, in a variety of ways, such as:

- ✓ An increase in intestinal absorption
- ✓ Drug metabolising enzymes are inhibited, which prevents the liver and intestines from breaking down medicines (inhibiting first pass mechanism of destruction of drugs)
- ✓ By blocking efflux pumps, the drug's absorption in the gastrointestinal tract and through the bile is slowed.
- ✓ An increase in the pathogen medicines' permeability.
- ✓ Blocking the defence mechanisms of pathogens or cancer cells (such as medicine efflux)
- ✓ More ways to interact with the pathogenic binding affinity (such as DNA and proteins)
- ✓ Increasing the blood-brain barrier's permeability.

CONCEPT OF BIO-ENHANCERS

Herbal bio-enhancers have their origins in the traditional Ayurvedic medical system. Between the 7th century B.C. and the 6th century A.D., people utilised the Ayurvedic "Trikatu," which is a Sanskrit word that meaning "three acrids." The active ingredient piperine, which is found in a blend of black pepper (Piper nigrum Linn.), long pepper (Piper longum Linn.), and ginger (Zingiber officinale Rosc.), helps the body absorb medications, minerals, and vitamins.[6] Enhancement of bioavailability, as depicted in Fig.1

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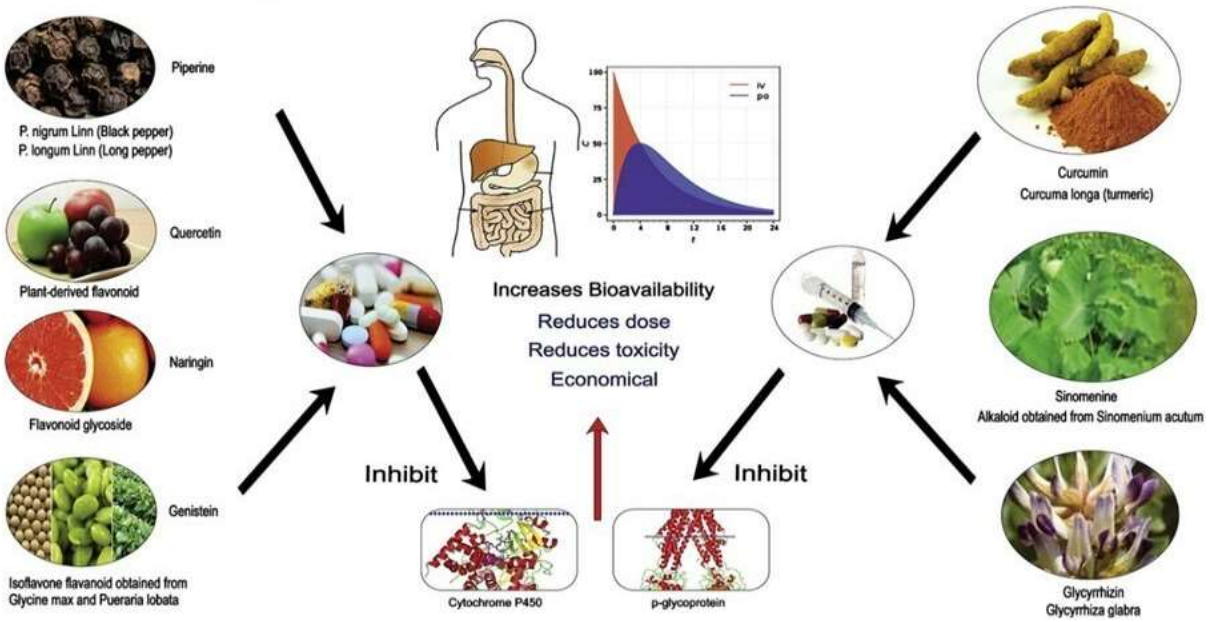

Figure 1: Enhancement of bioavailability

CONCEPT IN AYURVEDA[7]

In contemporary medicine, soluble enhancers are a relatively recent development. This idea first appeared in the Ayurvedic medical system, which has been using it for many years. Bio-enhancers increase bio-availability or bioactivity when combined with the main medication at low dosages. Zingiber officinale Rosc., Piper longum Linn., and Glycyrrhiza glabra Linn. have all been employed in Ayurveda for bio-enhancers and different phytomethods from ancient times. By sharing the expense of therapy, bio-enhancement lowers the therapeutic dosage of the primary medication, minimising the risk of toxicity and adverse effects while also increasing efficacy, lowering tolerance, and reducing the amount of raw materials needed to produce the drug. A variety of Ayurvedic medications and techniques for increasing bioavailability are the topic of this review paper.

Piperine[8]

A variety of foods and medications have increased bioavailability thanks to piperine, a natural alkaloid present in P. nigrum Linn (black pepper) and P. longum Linn (long pepper). It has been used for a very long time as a spice and flavouring in a variety of savoury meals. Many ailments, including seizure disorders, have been treated with piper species in traditional medicine. Piperine exhibits a number of biological effects, such as anti-inflammatory, antipyretic, fertility-improving, anti-fungal, anti-diarrheal, antioxidant, anti-metastatic, anti-thyroid, anti-mutagenic, anti-tumor, anti-depressant, anti-platelet, analgesic, hepatoprotective, anti-hypertensive, and anti-asthmatic properties. Piperine has immunotoxic and reproductive effects on Swiss albino mice as well as being toxic to hepatocytes and cultured hippocampal neurons. Piprine as depicted in Figure 2.

Zingiber Officinale[9]

Zingiber officinale (Ginger) rhizome extract contains active gingerols, which can be converted to shogoals, zingersingle and paradol. These compounds are the main sources of a

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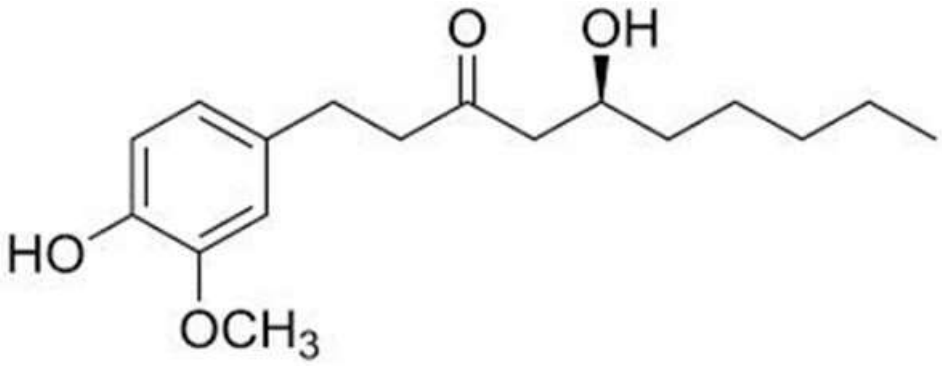
substances pungent qualities. The volatile oil in ginger, which has a yield of 1 to 3%, is chiefly responsible for the spice's aroma. In Gingerols have gastrointestinal motility improving, sedative, antipyretic and antibacterial effects in laboratory animals. Gingerol is the primary pungent component of ginger. Gingerol may one day replace dangerous and expensive treatments due to its chemoprotective properties. Analgesic and antipyretic effect, antiulcer, antithrombic, bacterial, fungal, anti-inflammatory, anti-hyperglycemic, anti-iemic, anti-malerial, antioxidant and anti-apoptotic activity and anticancer activity are some of ginger's benefits. Ginger has an effect on the mucous membrane of the digestive system. Ginger's job is to regulate intestinal activity and enhance absorption.



Niaziridin[10]

It has been revealed that Drumstick leaves, pods, and bark contain niaziridin, a nitrile glycoside (Moringa oleifera). The anti-fertility, anti-microbial, diuretic, anti-cancer, anti-inflammatory, hypotensive, anti-spasmodic, anti-fungal, anti-ulcer, anti-oxidant, hepatoprotective, hypolipidemic, anti-teratogenic, and anti-arthritic properties of M. oleifera have been demonstrated. Both Gram-positive and Gram-negative bacteria, such as M. smegmatis and Bacillus subtilis, have shown increased bioactivity in response to antibiotics including rifampicin, ampicillin, tetracycline, and nalidixic acid. When used against Gram-negative bacteria like E. coli, it increases the effectiveness of antibiotics including rifampicin, ampicillin, tetracycline, and nalidixic acids. Rifampicin, penicillin, tetracycline, and nalidixic acids all have a 1.2–19-fold increase in their ability to combat Gram-positive germs. It increases the effectiveness of azole antifungal medications like clotrimazole against Candida albicans by 5–6 times.

Glycyrrhizin

Liquorice plants contain the glycoside glycyrrhizin in their roots and stolons (Glycyrrhiza glabra). As an expectorant, it aids in the treatment of bronchitis, allergies, asthma, gastritis, peptic ulcers, rheumatism, and sore throats. It helps the liver detoxify medicines and is used to treat liver diseases. It strengthens the immunological system, stimulates the adrenal glands, and has diuretic and laxative properties. 50 times sweeter than sucrose is glycyrrhizin. The most common uses are for the treatment of respiratory and intestinal channels, as well as peptic ulcers and other stomach disorders. Glycyrrhizin has a number of beneficial effects, including anti-inflammatory, anti-cancer, anti-viral, and anti-hepatotoxic effects.[11]

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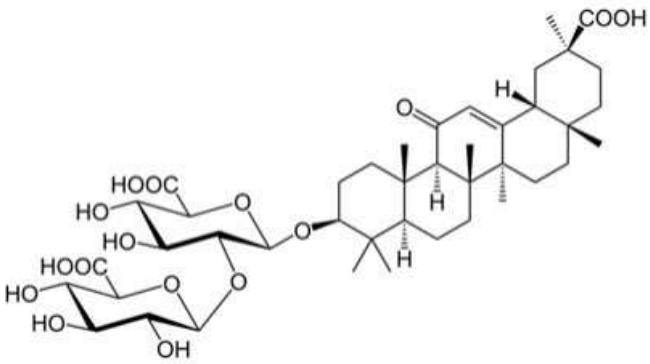
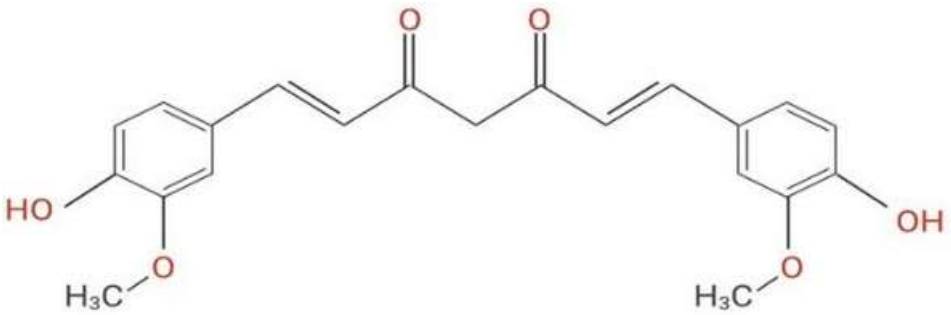


Allicin

Garlic contains a chemical called allicin, which contains allyl sulphur (Allium sativum). Anti-platelet activity, anti-oxidant activity, anti-bacterial activity, anti-cancer characteristics, immunomodulatory effect, anti-diabetic activity, anti-parasitic activity, anti-microbial activities, anti-oxidant and antiaction and virucidal are only a few of allicin's attributes.[12]

Curcumin

Curcumin, a common Indian spice, is the primary curcuminoid found in turmeric (Curcuma longa). Curcumin raises the end AUC of celiprolol and temazepam in rats by inhibiting the drug metabolising enzymes (CYP3A4) in the liver, which changes the drug transporter P-glycoprotein.[13]



Lysergol

The Morning Glory Plant (Ipomoea spp.) produces lysergol, a phytomolecule that could be used as a herbal bioenhancer to boost the effectiveness of antibiotics in killing bacteria**.** Higher species like Rivea corymbosa, Ipomoea violacea, and Indigofera muricata must have been used to isolate it. The bio-enhancing properties of lysergol are being studied. Lysergol has a recommended dosage level of 10 g/ml as a bioenhancer and solubility enhancer. Several medications, including rifampicin, tetracycline and ampicillin have higher bioavailability. The antibacterial effects of an antibiotic are increased by 2-12 times by lysergol.[14]

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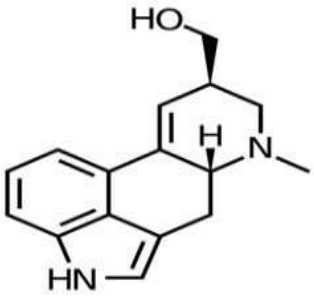

Aloe vera gel and whole leaf extract

The morning Glory plant (Ipomea spp.) producer's lysergol, a phytomolecule that improves the effectiveness of antibiotics in killing germs. Higher species like Rivea corymbosa, Ipomoea violacea and Indigofera muricata must have been used to isolate it. The bio-enhancing properties of lysergol are being investigated. lysergol has a recommended dosage level of 10 g/ml as a bio-enhancer and bio-availability enhancer. Many medications, including rifampicin, tetracycline and ampicillin have enhanced bioavailability. An antibiotic's antibacterial activity is increased by 2-12 times by Lysergol.[15]

Capsaicin

The substance that makes chillies active is capsaicin (Capsicum annum).Mammals, especially humans are irritated by it and any time tissue comes into contact with it. It causes tissue to burn. Following oral treatment, capsicum annum decreases the Bioavailability of aspirin in rats but has little to no effect on the bioavailability of ciprofloxacin.[16]

Bio-Availability/Bioefficacy-Enhancing Activity

"A substance at a lower dosage level that, when combined with a medication or carbohydrate delivers increased accessibility of the drug by reducing the utilization of the medication or nutrient, resulting to enhanced efficacy of the pharmaceuticals," is the defination of bioactivity of "bioenhancing activity."

Since they are:

(1) Difficult to obtain, a large number of medications have a strong interest in enhanc
ing bioavailability.

(2) Used for an extended period of time,

(3) Toxic

(4) Expensive.

Since plasma concentrations and consequently, therapeutic effects are directly impacted by bio-availability. Bioavailability is significant in the medical sector. An increase in bioavailability can reduce the recommended dosage of drugs, making price medications more accessible and minimising negative side effects. Because a considerable amount of a dosage never reaches the plasma or has time to exercise its pharmacological effects, poorly bioavailable medications continue to sub-therapeutic. Any significant increase in bioavailability will result in decrease in the drug's dosage or frequency of administration. For a medication with a limited safety margin, intersubject variability is especially alarming. Poor intestinal membrane permeability, drug breakdown in gastric or intestinal fluids, poor disintegration or low water solubility, and presystemic intestinal or hepatic metabolism can

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all contribute to inadequate oral bioavailability. Numerous therapeutic methods used during treatment cause the loss of essential neutraceuticals. By enhancing the bioavailabity and bioefficacy of certain nutritional supplements such as metals and vitamins, bioenhancers enhance nutritional status.[17]

The following substances can be applied to increase bioavailability:

a) Increasing the GI tract's ability to absorb medication.
b) Slowing down or preventing the biotransformation of medications in the liver or intest ines.
c) Altering the immune system in a way that considerably reduces the overall need for th e medicine.
d) Increasing pathogen entry or penetration, especially when pathogens have persistor pr operties within macrophages, as is the case with Mycobacterium tuberculosis and othe r pathogens. As a result, areas where the active medicine would otherwise be inaccessible are properly guarded for the improved eradication of these organism.
e) Preventing pathogens or abnormal tissue from rejecting the treatment, as in the case with efflux mechanisms that are frequently present in antimalarial, anticancer and antibacterial medications.
f) Altering the channel of communication between

a) Increasing antibiotic activity against pathogens by enhancing the drug's adheren ce to particular pathogen components, such as sensors, proteins, DNA, RNA, and similar structures.
b) In addition to the previously described mechanism of action, bio-enhancer compounds may be helpful in accelerating the passage of nutrients and medications across the blood-brain barrier, which may be extremely helpful in the treatment of disorders like ce rebral infections, epilepsy, and other CNS problems.

Modern medicine development employs a range of techniques to increase bioavailability, incl uding:

a) Chemical modification to make the medication more polar.
b) Salt preparation or complexation.
c) Production of drugs.
d) The terms micronization and nanonization are interchangeable
e) The choice of particular polymorphic forms.
f) Drug distribution to the site of action with precision.
g) Film coating enables carefully regulated medication delivery.
h) The creation of polymorphic matrices makes it possible for drugs to leak s lowly over time.
i) Liposomal microencapsulation and other procedures that are comparable.
j) The use of P-glycoprotein inhibitors.[18,19]

However, from ancient times, there has been widespread support for the idea that increasing b ioavailability by combining a secondary agent with the primary therapeutic treatment.

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However, using herbal bioenhancers to increase a drug's bioavailability is a novel strategy ba sed on Ayurvedic literature [20], particularly for medications with low bio-availability.

Pharmaceuticals with considerable bioenhancement include those for the cardiovascular, pul monary, CNS, GIT, immune, and anticancer systems.
Tetracyclines, sulfadiazine, vasicine, rifampicin, pyrazinamide, ethambutol, phenytoin, pheno barbital monohydrate, carbamazepine, nimesulide, indomethacincarotene, coenzyme, ciproflo xacin, curcumin, dapssingle, amino acids, glucose, and a number.

MECHANISMS OF ACTION

A variety of techniques are used by herbal bio-enhancers to achieve their results. Herbal bio-enhancers may function in a same or different ways**.**
They promote medical bioavailability by influencing drug metabolism, whereas theyincrease nutritional bioavailability by encouraging absorption in the gastrointestinal system.
On the other hand, fluids had a negligible impact on GE at the same dosage.A singleweek ora l administration of 1 mg/kg and 1.3 mg/kg did not produce any diffrences from a single-dose treatment.
Thermoreceptor activation, catecholamine release, and direct beta 1, 2, and 3 adrenoceptor agonist activity are hypothesised to initiate thermogenesis and bioenergetic path ways.
Additionally, ATP can control catecholamine synthesis through P2 type purinergic receptors, and the compositions of the invention can directly or indirectly sti mulate dopaminergic and serotonergic systems. This may have a part in thermogenesis and an increase in lean body mass, as well as having anti-obesity and anti-diabetic properties.
The plasma concentrations of triiodothyronine (T3) and thyroxine (T4), as well as an increase in tissue oxygen consumption and thermogenesis, could all increase with an increase in thyro id peroxidase activity, an essential enzyme in thyroid hormone synthesis.[21] The status of gluta myl transpeptidase activities, amino acid absorption, and lipid peroxidation were examined in piperinemediated changes in the permeability of rat intestinal epithelial cells.
It was investigated how piperine affected the gut's capacity for absorption.
Piperine (25-100 M) increased -glutamyl transpeptidase activity, radioactively tagged l-leucine, lisoleucine, and lvaline absorption, as well as lipid peroxidation in newly separated e pithelial cells of the rat jejunum, according to in vitro studies. Piperine maintained its improv ed glutamyl transpeptidase activity in the presence of benzyl alcohol. According to these inve stigations,[22] piperine interacts with the lipid environment to produce effects that increase inte stinal cell permeability..

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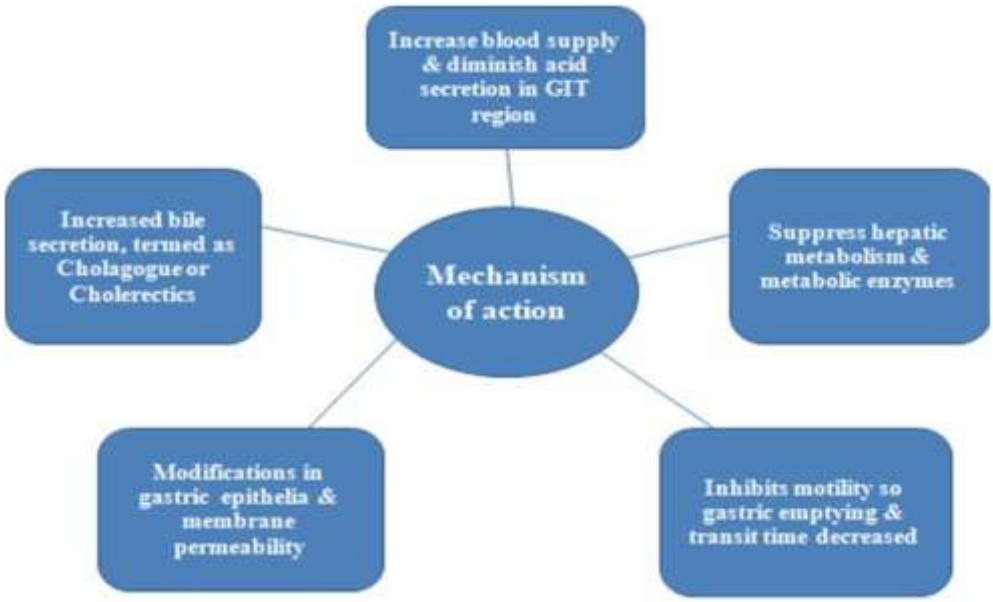

TABLE 1: BIOENHANCMENT TECHNIQUES[23]

Physical modification	Chemical modification	Other methods
A. Particle size reduction: 1. Micronization 2. Sonocrystalisation 3. Nanosuspension 4.Supercritical fluid process	Change in pH	Co-crystalisation
B. Modification of crystal habit: Polymorphs, Pseudo polymorphs.	Use of Buffer	Co-solvency
C. Drug dispersion incarries 1.Eutectic mixtures 2.Solid dispersion 3.Solid solutions.	Derivatisation	Hydrotrophy
D.Complexation use of complexing agent:		Solubilizing agents
E. solubilisation by surfactants microemulsions		Selective adsoption oninsoluble carrier

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SIGNIFICANCE OF BIO-ENHANCERS: [24,25]

Decreased dosage

A smaller oral medicine dosage is needed to attain the desired blood levels because bio-enhancers increase the amount of medication reaching the blood circulation and prevent phar maceuticals from being squandered inside the body.

Decreased raw material usage

Reduced dosage requirements for desired pharmaceutical action have a positive effect on the quantity of raw materials needed to create drugs, saving any nation a considerable amount of money.

Environmental friendly

Fewer trees or plants are needed in the production of expensive and uncommon tree-based medications, such as Taxol, an expensive anti-cancer medication derived from slow-growing yew trees. This is advantageous for the environment.

Cost effective

Medication costs are already decreased by the dosage reduction.

Insufficient medication bioavailability costs various nations hundreds of billions of dollars, pl acing a heavy financial burden on any nation, but especially poor emerging nations.

This is particularly true for dangerous and feared diseases like tuberculosis, whose expensive, harmful, and urgent treatment has prompted the UN to proclaim an emergency situation due t o the spread of AIDS and the advent of major drug resistance.

Less side effects

Drug side effects are also decreased as a result of the decreased dosage. Improved compliance

Enhancing drug tolerance, compliance, and treatment completion are all benefits of reducing side effects.

Decreased resistance of drug

The possibility of hazardous medication resistance emerging is diminished solely by the impr oved tolerability and compliance.

Added hepatoprotective and gastro protective actions

Despite the fact that bioenhancers lack pharmacological activity, they can still provide additio nal benefits, such as reducing the gastrointestinal side effects and hepatotoxicity of the primar y active drug, improving formulation safety and tolerability, and reducing drug toxicity and r esistance.

For instance, lowering the dosage of the expensive, lethal drug Rifampicin reduces its cost an d adverse effects by 60% when used to treat the dreaded disease tuberculosis.

This is a major benefit for poor patients, poor nations, and awful human diseases.

APPLICATIONS [26,27]

Candidates for bioenhancer technology include pharmaceuticals with high toxicity, high cost, rare medications, low bioavailability, and medications that must be taken for extended period s of time. However, it can be utilised in any medication that contains bio-enhancers.

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Several patent applications have been filed as a result of the discovery and characterisation of bio-enhancers.

With vitamins, curcumin, resveratrol, and Coenzyme Q10 as a bioenhancer, piperine is availa ble in mono formulations.

CONCLUSION

In developing nations, the price of therapy has long been a significant issue. Researchers have been working to make therapy more widely available to the public. Environmental changes ty pically have a positive effect on a nation's economy by reducing prescription dosage and rese arch costs. When a bioavailable medicine is taken in high doses, toxicity is decreased. Additi onally, it gets rid of drug resistance and cuts down on treatment time in half. Because it is nat ural, it is riskfree, easily accessible, nontoxic, and without any negative side effects. Thus, a v ariety of potent medications' bioavailability can be increased by combining a number of natur al substances. It's probable that the formulation's objective is to combine the drug with an extr emely potent enhancer.

REFRENCES

1. Randhawa GK, Singh J, Kullar R. “Bioenhancers from mother nature and their applicability in modern medicine”. Int. j. appl. basic med res. 2011, 1(1), 1-5.
2. Atal CK. “A breakthrough in drug bioavailability-a clue from age old wisdom ofAyurveda.” IDMA Bulletin. 1979, 10, 483.
3. Badmaev V, Majeed M, Norkus EP. “Piperine, an alkaloid derived from black pepper increases serum response of beta-carotene during 14-days of oral beta-carotene supplementation.” Nutr. Res. 1999, 19(3), 381-388.
4. Zutshi RK, Singh R, Zutshi U, Johri RK, Atal CK. “Influence of piperine on rifampicin blood levels in patients of pulmonary tuberculosis.” JAPI. 1985, 33(3), 223-224.
5. Dr.C.K. World's first bio-enhancer Piperine. Atal conferred the EDPA award of appreciation for outstanding contributions in drug development and Piperine research, EDPA, 2014, 27.
6. Khanuja S, Arya J, Srivastava S, Shasany A, Kumar TS, Darokar M, Kumar S, inventors; Council of Scientific, Industrial Research CSIR, assignee. Antibiotic pharmaceutical composition with lysergol as bio-enhancer and method of treatment. United States patent application US 11/395,527. 2007.
7. Singh S, Tripathi JS, Rai NP. An appraisal of the bioavailability enhancers in Ayurveda in the light of recent pharmacological advances. Ayu. 2016, 37(1), 3.
8. Badmaev V, Majeed M, Norkus EP. Piperine, an alkaloid derived from black pepper increases serum response of beta-carotene during 14-days of oral beta-carotene supplementation. Nutr. Res. 1999,19(3), 381-388.

ISSN PRINT 2319 1775 Online 2320 7876

 UGC CARE Listed (Group -I) Journal Volume 11, Iss 12, 2022

9. Govindarajan VS, Connell DW. Ginger—chemistry, technology, and quality evaluation: part 2. Crit. Rev. Food Sci Nutr. 1983, 17(3):189-258.
10. Shanker KK, Gupta MM, Srivastava SK, Bawankule DU, Pal A, Khanuja SP. Determination of bioactive nitrile glycoside (s) in drumstick (Moringa oleifera) by reverse phase HPLC. Food chem. 2007, 105(1), 376-382.
11. Kiso Y, Tohkin M, Hikino H, Hattori M, Sakamoto T, Namba T. "Mechanism of antihepatotoxic activity of glycyrrhizin, I: effect on free radical generation and lipid peroxidation." Planta med. 1984, 50(04), 298-302.
12. Makheja AN, Bailey JM. 1990 "Antiplatelet constituents of garlic and onion. Agents and actions." Springer publications.
13. Zhang W, Tan TM, Lim LY. "Impact of curcumin-induced changes in P-glycoprotein and CYP3A expression on the pharmacokinetics of peroral celiprolol and midazolamin rats." Drug Metab Dispos. 2007, 35(1):110-5.
14. Patil S, Dash RP, Anandjiwala S, Nivsarkar M. "Simultaneous quantification of berberine and lysergol by HPLC- UV: evidence that lysergol enhances the oral bioavailability of berberine in rats." Biomed Chromatogr. 2012; 26(10), 1170-1175.
15. Vinson JA, Kharrat H, Andreoli L. "Effect of Aloe vera preparations on the human bioavailability of vitamins C and E. Phytomedicine." 2005, 12(10), 760-5.
16. L Cruz, HG Castañeda. "Navarrete A. Ingestion of chilli pepper (Capsicum annuum) reduces salicylate bioavailability after oral aspirin administration in the rat." Can. J. physiol. pharmacol. 1999, 77(6), 441-6.
17. Qazi GN, Bedi KL, Johri RK. "Bio-availability enhancing activity of Carum carvi extracts and fractions there of," United state Patent. WIPO W02004067018, 2004, 1-6.
18. Breedveld P, Beijnen JH, Schellens JH. "Use of P-glycoprotein and BCRP inhibitors to improve oral bioavailability and CNS penetration of anticancer drugs." TIPS. 2006, 27(1), 17-24.
19. Khan IA, Mirza ZM, Kumar A, V Verma, GN Qazi . "Piperine, a phytochemical potentiator of ciprofloxacin against Staphylococcus aureus." Antimicrob agents chemother. 2006, 50(2), 810-2.
20. Bajad S, Bedi KL, Singla AK, Johri RK. "Piperine inhibits gastric emptying and gastrointestinal transit in rats and mice." Planta medica. 2001, 67(02), 176-9.
21. Majeed M, Badmaev V, Rajendran R, inventors; Sabinsa Corp, assignee. "Use of piperine as a bioavailability enhancer." United States patent, US5744161A, 1998.
22. Johri RK, Thusu N, Khajuria A, Zutshi U. "Piperine-mediated changes in the permeability of rat intestinal epithelial cells: the status of γ-glutamyl transpeptidase activity, uptake of amino acids and lipid peroxidation."

ISSN PRINT 2319 1775 Online 2320 7876

 UGC CARE Listed (Group -I) Journal Volume 11, Iss 12, 2022

Biochem Pharmacol. 1992, 43(7), 1401-7.

23. Varun RV, Venkateshwarlu L, Srikanth L. "Solubility enhancement techniques. Int. J. Pharm. Sci. Res. 2010, 5, 41-51.
24. Randhawa GK, Jagdev SK. "Bioenhancers from mother nature and their applicability in modern medicine." Int. j. of appl. basic med. res. 2011, 1(1), 5.
25. Atal CK, Dubey RK, Singh J. "Biochemical basis of enhanced drug bioavailability by piperine: evidence that piperine is a potent inhibitor of drug metabolism." JPET. 1985, 232(1), 258-62.
26. Atal N, Bedi KL. "Bioenhancers: Revolutionary concept to market." J-AIM. 2010, 1(2), 96.
27. Choudhary N, Khajuria V, Gillani ZH, Tandon VR, Arora E. "Effect of Carum carvi, a herbal bioenhancer on pharmacokinetics of antitubercular drugs: A study in healthy human volunteers."PICR. 2014, 5(2), 80.