BIOENHANCERS – A NEW APPROACH IN MODERN MEDICINE

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ARTICLE INFO

Article history
Received 19/12/2013
Available online 31/12/2013

Keywords
Bioavailability, Bioenhancer, Modern Medicine, Absorption, Dosage Forms.

ABSTRACT

Bioenhancers or biopotentiators are a revolutionary concept in modern medicine. Bose in 1929 reported this for the first time on the antihistaminic effects of Vasaka leaves. Its effect was increased by the addition of long pepper in it.

Outcomes: Large number of drug compound has been introduced by the advances in drug designing technologies. By co-administering drugs with naturally occurring compounds from plants which are considered to be simple and safe, can increase the bioavailability of drugs. With modern medicine, Ayurveda can be combined which can make major contribution to the drug discovery process through reverse pharmacology by identification of active compounds and reduction of drug development costs.

Conclusion: By this Ayurveda based technology, bioavailability of drugs can be increased and this has made a revolutionary change in the way medicines are administered.

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Please cite this article in press as X.Fatima Grace et al. Bioenhancers – a new approach in modern medicine. Indo American Journal of Pharm Research. 2013:3(12).

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INTRODUCTION

About 60% of the world population use plant-based medicines and about one third of the world countries depend on herbal medicines[1]. A bioenhancer is an agent which is used to enhance the bioavailability and efficacy of a drug with which it is co-administered, without any pharmacological activity of its own at the therapeutic dose used[2,3]. They have the tendency to decrease the dose of active drug.

Many drugs both synthetic and herbal drugs face a problem of reduced Bioavailability, which is the rate and extent of drug entering systemic circulation and becomes available at the site of action[4-6]. Maximum Bioavailability is attained by drugs administered intravenously, whereas drugs administered orally usually undergo first pass metabolism and are poorly bioavailable due to incomplete absorption. Such drugs which have not been utilised by the body may lead to drug resistance and adverse effects. The best way to achieve reduction in drug dosage and thereby drug toxicity and cost is by increasing the drugs Bioavailability[7-9]. One of the ways of increasing the Bioavailability of drugs is by addition of molecules which do not have similar therapeutic activity but increase the Bioavailability when incorporated in the formulation of another drug. These are called as Bioenhancers and they do not show synergistic effect with the drug[10-12].

Modern researchers show increased interest in the enhancement of Bioavailability of most of the drugs by addition of various herbs with bioenhancing property.

To achieve bioenhancing property of a drug various approaches are adopted for instance by using absorption enhancers, prodrugs, micronisation, and manufacturing of delayed release, sustained release capsules and spansules, permeability enhancing dosage forms like liposomes and emulsions[13].

AYURVEDA – YOGVAHI

In Ayurveda, the concept of bioenhancer is termed as Yogvahi. It is used to enhance Bioavailability, tissue distribution, increase efficacy of drugs especially drugs with poor Bioavailability. Specific yogvahis or bioenhancers are called as Anupaan and Sehpaan[14-16].

ANUPAAN

This means food concomitantly given with medicament to increase the effect of medicament. For example: Amrit Dhara drops. It is used in gastrointestinal diseases. These drops are taken after they are put over sugar to increase their potency.

SEHPAAN

This means vehicle used during the manufacture of dosage forms to increase the effect of the drug. For example: Panchgavya prepared using ghee or clarified butter to increase its effect.

Examples of yogvahis generally used in ayurvedic formulations are Piper longum, gold, cow urine distillate, etc.,

PROPERTIES OF BIOENHANCER

The bioenhancers used in formulation should comply with the following properties like[17-19]

- It should be non-toxic
- It should be effective at very low concentration
- Should be easy to formulate
- Should enhance the activity of the drug molecules
- Should not possess any pharmacological activity of its own at the therapeutic dose used.

CLASSIFICATION

Bioenhancers are broadly classified[20-23] depending on two parameters

1. Based on Origin
2. Based on Mechanism of Action

1. Based on Origin

This is further classified into plant and animal origin.

Few examples for plant origin: Stevia, Piperine, Capsaicin, Allicin, Ginger, etc.

An example for animal origin: Cow urine distillate.

2. Based on Mechanism of Action

- Inhibitors of P-gp efflux pumps
  Example: Carum carvi, Genistein, Sinomenine
-Suppressors of Cyp -450 enzyme and its isoenzymes
  Example: Naringin, Gallic acid, Quercetin
- Regulators of GIT function to facilitate better absorption
  Example: Aloe, Niaziridin, Ginger, Liquorice.

MECHANISM OF ACTION

There are several mechanisms of actions by which bioenhancers act. Different bioenhancers have different or same mechanism of action[24,25].

For example Nutrition bioenhancers enhance absorption by acting on GIT.
Antimicrobial bioenhancers act on drug metabolism process.

Bioenhancing activity of herbal compounds is attributed to many mechanisms, like inhibition activity of P-gp by flavone, quercetin, and genistein, inhibition of efflux transporters, like P-gp and breast cancer resistance protein (BCRP) using naringin and sinomenine thus preventing drug resistance; DNA receptor binding, modulation of cell signaling transduction, and inhibition of drug efflux pumps by stimulating leucine amino peptidase and glycy1-glycine dipeptidase activity, thus modulating the cell membrane dynamics related to passive transport mechanism as seen with piperine[26]; nonspecific mechanisms, like increased blood supply to the gastrointestinal tract, decreased hydrochloric acid secretion, preventing breakdown of some drugs; and inhibition of metabolic enzymes participating in the biotransformation of drugs, thus preventing inactivation and elimination of drugs and thereby, increasing their bioavailability[27].

**BENEFITS**

Use of Bioenhancers pose the following benefits[28] to the world population

- Reduced drug dosage.
- Reduced cost of drug.
- Reduced resistance of drug.
- Reduced adverse drug reaction or side effects.
- Increased efficacy
- Increased Bioavailability
- Decreases requirement of raw material for drug manufacture.
- Economically benefitted to the world economy.
- Decreases treatment cost.

**HURDLES**

Bioenhancers in drug delivery have been successful but not all the approaches have been met with all success[29]. The newly developed Bioenhancers have many challenges to be faced.

- To improve the properties of drug formulation like circulation in blood, increased functional surface area, protection of drug from degradation, crossing biological barriers & site specific targeting.
- The Research & development of herbal Bioenhancers in large scale production is a probelm. It is easy for pilot scale production than the large scale production.
- The next posed problem is on regulatory control. There is a need to have regulations for physicochemical & pharmacokinetic properties of newer bioenhancers than the other conventional drug products.

**FUTURE PERSPECTIVES**

As a lead to Bioenhancers[30], the use of piperine as bioenhancers in various modern medicines to increase their bioenhancers has been applied. The concept of Anupaan & Sehpaan can be also incorporated into modern medicine. Many other bioenhancers can be developed from natural sources such that cost & dose of the drug can be decreased, thereby reduce side effects of the drug.

**CONCLUSION**

Bioenhancers propose a newer concept in the discovery based on traditional system of Indian medicine. The improvements in this concept will definitely lead to reduction in cost of drug, toxicity, other adverse effects and will have a beneficial influence on the economy of the country. It is safe, effective, economical, easily procured, non additive too[31].

Thus, the approach of bioenhancer in modern medicine is very essential today and the development of bioenhancers from other sources has become need of the hour.

**ACKNOWLEDGEMENT**

The authors are thankful to the management of Sri Ramachandra University for their constant support and encouragement towards the completion of work.
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