

# “Yogvahi (Bioenhancer)”: An Ayurvedic Concept Used in Modern Medicines

S. H. Majumdar, A. S. Kulkarni, S. M. Kumbhar

Pharmaceutics Department, Shivaji University, Kolhapur, Maharashtra, India-415004

Email address: majumdarshiv@gmail.com

**Abstract**—“Bioenhancers” a revolutionary concept is well known in modern medicine that are used to efficacy of drug(s). The concept was researched and tested in various modern medicines, but its roots are general somewhere from classical system of Medicine (Ayurveda). This concept was known as Yogvahi in Ayurveda. Raw spices and herbs help with their aroma too, but Ayurveda recommends cooking the spices and herbs. These spices and herbs are mentioned as a Yogvahi in Ayurveda which principally serves as vehicle for nutrients in food, so these are essential in our diet but we forget to use them, we just include them in different recipes as a flavouring agent. Trikatu, bhasmas, cow urine distillate etc are notable findings of Ayurvedic Yogvahis.

In modern medicines, formulation of many molecules, as piperine and quercetin, is considered as scientific usage. Anti-tubercular therapy consists combination of rifampicin, isoniazid, and piperine is an example of this. Along with such breakthrough as outputs, there is few failure cases are also reported. For getting proper breakthrough, systemic approach that can co-relate classical approach with modern principles that the most possible reason where due combination with drugs reduces the economic tag of costly drugs. This paper relates to the co-relation between the ancient concept and its applicability in modern medicines.

This article decodes the core concept of Ayurveda and opens the secrete of ancient science of health.

**Keywords**—Bioenhancers; Yogvahi; Ayurveda; Modern medicine; bioavailability.

## I. INTRODUCTION

Newly developed technical aspects of identifying new entity with various mode of action are been designed nowadays. In addition, economical aspects are taken into consideration for development of drug due to which cost of medicine are becoming cheap. The parameter such as bioavailability is thoroughly studied. Hence, for the treatment of the cost of drug could be successfully get decreased. In 2000, the WHO published a book on the economic evaluations of healthcare services.

Ayurveda has played a foremost role to drug discovery process in the course of reverse pharmacology, with innovative method of identifying effect of drugs. Advanced technique for growth and development of another Ayurvedic formulation enhancing bioavailability of drugs, have produced a drastic changes in the way medicines are administered. The scenario of scheme aimed to decrease drug dosage, and drug treatment expenditure<sup>1,2</sup>.

## II. WHAT ARE BIOENHANCERS?

Bioenhancers are substances from nature which do not have their own typical therapeutic activity at the dose use. When it is combined with drug it increases bioavailability and bioefficacy of specified drug and leads to potentiation of pharmacologic effect of that drug. It do not have its own therapeutic effect at dose used<sup>3,4,5</sup>.

There are two concepts related to *Yogvahi*-

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

E.g. Amritdhara drops

Used in gastrointestinal diseases, by putting drops over sugar to increase potency

2. **Shepaan**: means vehicle, which is used during manufacturing of medicament.

E.g. Brahmi ghrita

In which Brahmi is used as drug and ghee as a vehicle which increases effect of Brahmi<sup>6</sup>.

### Origin of Bioenhancers:

Bioenhancers is an ancient term of “Ayurveda” which implies the increase effect of drug in combination with it. Ayurveda terms it as “Yogvahi” in Sanskrit which indicates increase in effect by combination. In 1929, Bose has documented action of bioenhancer. He has used long paper to increase antihistaminic property of vasaka<sup>4</sup>.

Another scientist C. K. Atal has scientifically estimated piperine as first bioenhancer in 1979, work is done at Regional Research Laboratory, Jammu (Indian Institute Of Integrative Medicines) in ayurveda Trikatu i. e. black paper (*Piper nigrum*), long paper (*Piper longum*) and ginger (*Zingiber officinale*) is used widely, so Mr. Atal put hypothesis that Trikatu increases efficacy. When he studied all ingredients, he found piperine i.e. active constituent in *Piper longum* increases bioavailability of many drugs, so according to its work to enhance bioavailability ‘bioenhancer’ term was coined<sup>4,5,7-10</sup>.

### Need of bioenhancers:<sup>11</sup>

To pass biological membrane molecules have to pass – solubility and molecular size. Molecules having poor lipid solubility and improper molecular size or both give poor absorption and poor bioavailability.

Bioenhancers increases penetration through membranes and helps to solve problem of poor absorption and poor bioavailability.

### Benefits of using bioenhancers:<sup>12</sup>

- As it increases bioavailability drug dose can be reduced
- Due to reduced dose cost will also reduce

- It reduces drug resistance
- Also reduces side effects and adverse drug reactions
- It increases efficacy of drug
- In short decreases total treatment cost

#### Ideal properties of bioenhancers: <sup>11</sup>

- It must be nontoxic
- It must be effective at very low concentration
- Easy to formulate
- Compatible with API and excipients
- It should not show any pharmacological activity at the therapeutic dose used
- It should be free from any toxic /harmful effect on body

#### Bioenhancers in modern medicine:

The work done in this area so far explains that tradition of Ayurveda can be the new scope in enhancing the bioavailability of allopathic drug which have proven pharmacotherapeutics action. Hence the utilization of this phenomenon is done for drug having poor bioavailability. So the hope in modern science and industrial impact come together to reap the formulating propaganda of drugs for development in human health care. Drugs in tuberculosis therapy like 'Risorine' by candida Pharma (Nov.2009) which contains rifampicin and isoniazid it has piperine as a bioenhancer, which shows evidence of increasing bioavailability <sup>6, 13, 14, 15</sup>.

#### Bioenhancers in Ayurveda:

The term bioenhancer is termed as "Yogvahi" in Ayurveda.

Raw spices and herbs can help through their aroma too, but ayurveda recommends cooking of spices and herbs, because in cooking material is exposed to heat and molecular interaction between medium (oil/ghee) and spices causes interaction of active components it also sanitize unwanted toxic material present in raw spices and herbs. Cooking helps to access digestive system and other systems. Almost all spices and herbs acts as a vehicle for nutrients in food and are called as yogvahi, these helps through breakdown of protein, carbohydrates, fat when there is a need. These are essential in diet but we use them as a flavor in special recipes.

The use of bioenhancer may lead to synergistic effect which enhances effect and reduce side effects. This area seems to fit naturally with the complex operation of the human body. It seems reasonable that, to move this whole symphony in a more harmonious direction, it would be most effective with complex substances – with supplements that could affect the whole at once <sup>10</sup>.

Bioenhancers found in plants are piperine, allicine, curcumin, ginger, quercetin, naringin, genistein, caraway, black cumin, niaziridin, lysergol, liquorice, stevia, peppermint oil, aloe, sinnomenium acutum, gallic acid, capsaicin, capmul, ammoniac microflora, gingerol, nitrile glycoside, callistemon rigidus, ferullic acid <sup>3, 4, 10-12, 17-36</sup>.

#### Piperine: <sup>4, 6, 10, 11, 17, 19-22, 25-29, 31</sup>

Major plant alkaloid obtained from black paper and long paper acts by promoting rapid absorption of drug and nutrients and by inhibiting enzymes useful for biotransformation of drugs. Drugs enhanced using piperine includes diclofenac sodium, pentazocin, phenobarbitone, propranolol, theophylline, metronidazole, methotrexate, etoposide, 18-B-glycyrrhetic acid nateglinide, ibuprofen, resveratrol, fexofenadine, carbamazepin, nevirapine, phenytoin, cyclosporine A, nimesulide, vasicine, sparteine, ampicillin, norfloxacin, rifampicin, tetracycline, pyrizinamide, INH, epigallocatechin-3-gallate, sulfadizine, fexofennadine, curcumin, saquinavir, nelfonavir, lopropanavir, amprenavir, ritonavir, ofloxacin, ciprofloxacin, indomethacine, atenolol, oxytetracyclin, beta lactams, oxyphenyl butazone, midazolam, linarine, mercaptopurine.

#### Quercetin: <sup>4, 6, 17, 25, 26, 29, 35, 37</sup>

Mainly found in citrus fruits, vegetables, leaves and grains, acts by inhibiting CYP-450, Cyp3A4, affects transport of P-gp. Drugs bioenhanced using quercetin include paclitaxel, ranolazine, valsartan, clopidogrel, doxorubicin, etoposide, ironotecan, digoxin, green tea polyphenols, Pioglitazone, diltiazem, epigallocatechin, tamoxifen, Pioglitazone,

#### Naringin: <sup>4, 10, 26, 27, 29</sup>

This is flavanoid obtain in grapefruit, apples, onion and tea. Acts by inhibiting P-gp and CYP3A4 and decreases metabolism of diltiazem, verapamil, clopidogrel, tamoxifen, quinine, nimodipine, felodipine, 17- $\alpha$  ethinylestradiol, paclitaxel, saquinavir, cyclosporin A, nitrendipine, terfenadin, etc. which results in decreased drug dose and increased plasma drug concentration.

#### Genistein: <sup>4, 6, 10, 17, 27</sup>

This is isoflavanoid obtained by *Glycin max* and *pueraria lobata*. acts by inhibiting P-gp and MRP2<sup>1</sup> and BCRP<sup>2</sup> efflux functions: paclitaxel, epigallocatechin-3-gallate can be enhanced using genistein.

#### Sinomenine: <sup>4, 10, 11, 17, 26</sup>

This is an alkaloid obtained from *sinomenium acutum*. acts by decreasing efflux transport by P-gp. verapamil, quinidine, paeniflorin, digoxin are few drugs which can be bioenhanced using sinomentine

#### Curcumin: <sup>4, 9, 18, 21</sup>

This is obtained from *curcuma longa* widely used in antimicrobial and anticancer drugs. Acts by suppressing drug metabolizing enzymes and by inhibition of P-gp. example of drugs includes norfloxacin, celipropol, midazolam, docetaxel, midazolam, methotrexate.

#### Glycerhizine: <sup>10, 11, 17, 21, 26, 27,</sup>

This is saponin glycoside obtained from roots and stolons of *glycerhiza glabra*. acts by enhancing absorption and by inhibiting p-gp. rifampicin, tetracycline, aconitin, ampicillin,

clotrimazol, taxol, vitamin B<sub>1</sub>, B<sub>12</sub> and nalidixic acid are few drugs which can be bioenhanced using glycerhizine.

**Gingerol:** 4, 10, 11, 17, 21, 25-27, 29, 34, 35,

Obtained from ginger.acts by promoting intestinal activity, drugs can be bioenhanced using gingerol includes methotrxate, vitamin A, Azithromycin, cephalixin, cefadroxil, amoxicillin, cloxacillin, rifampicin, ethionamide, ketoconazol, zidovudine, pefloxacin, erythromycin and 5-FU.

**Carum Carvi:** 10, 11, 26

Caraway oil obtained by crushing seeds of *C.carvi*. acts by enhancing permeation and by inhibiting P-gp.drugs like rifampicin, INH, pyrizinamide, cycloserine, ethionamide, cefdinir, cloxacillin, amphoterecin B, zidovudin and 5-FU can be bioenhanced using c.carvi.

**Nitrile Glycoside:** 4, 6, 11, 26

Obtained by drum stick pods. Contains two active principles niaziridin and niazirin. Acts by enhancing penetration into pathogen anf by enhancing absorption too rifampicin, tetracycline, INH, amphicillin, vitamin B<sub>12</sub>, clotrimazol, nalidixic acid can be used to improve bioavailability using nitrile glycosides.

**Lysergol:** 4, 10, 11, 17, 26

This is phyto molecule obtained from plants like *Rivea corymbosa*, *Ipomoea violacea* and *Ipomoea muricata*, its also found in fungus *claviceps* and *rhizopus*.

Acts by promoting uptake from gastrointestinal membrane and cell membrane. Rifampicin, tetracycline, ampicillin, can be bioenhanced using lysergol.

**Black Cumin:** 10, 11, 17, 27

Also called as *cuminum cymium* linn, active principle content is luteolin, shows synergistic effect with piperine and ginger. It enhances bioavailability of rifampicin, cycloserin, ethionamide, cefadroxil, cloxacillin, flucanazol, zidovudine, 5-FU, erythromycin, cephalixin, amoxicillin, Ketoconazole, toconazol etc.

**Allicin:** 4, 10, 11, 21, 27

Alicin is obtained from *allium sativum*, it enhances bioavailability of amphoterecin B

**Aloe vera:** 4, 10, 11, 17, 27

Leaf extract of aloe is generally used, it enhances activity of Vitamin C and Vitamin E.

**Curcumin:** 10, 20, 26, 27

Curcumin is obtained from *curcuma longa*, it shows enhancing of docetaxel, norfloxacin, celiprolol, midazolam, methotrexate

**Capsaicin:** 10

Obtained from *capsicum*, bioavailability of theophylline is enhanced using capsaicin.

**Peppermint oil:** 10, 31

Cyclosporine is reported drug whose bioavailability can be enhanced using peppermint oil.

**Gallic acid:** 10, 28

It exerts synergistic effect with piperine. It enhances bioavailability of nifedipine and saquinavir.

**Capmul:** 6, 10

It contains glyceryl monocaprata, which enhances bioavailability of ceftriaxone and lacidipine.

**Niaouli oil:** 33

Also called as *melaleuca quinquenervia* or broad leaved paper bark.

**Sweet basil oil:** 34

Also called as thai basil, saint joseph's wort

**Chlorophytum borrvili annum:** 35

Also known as safed musali.

**Tulasi oil:** 36

Obtained from *oscimum sanctum*, acts as bioenhancer on naproxen, nimesulide.

**Clove Oil:** 37

It enhances bioavailability of carvedilol.

**Cinnamic acid:** 28

Obtained from cinnamon, it enhances bioavailability of saquinavir.

**Asparagus racemosus:** 39

Also called as *shatavari*/*shatamuli*/*kurilo*/*shatavar*. It contains asparginamine, *shatavirosides A*; *B*, *shatavarin*.

**Decanoic acid:** 39

Source: coconut oil, palm kernel oil, milk of various mammals or animal fats. patent is granted for the use of decanoic acid as a bioenhancer

**Silibinin:** 25

Also known as *silybin*. It acts as a bioenhancer for curcumin.

**Callistemon rigidus/stiff bottle brush:** 6

It acts as a bioenhancer for ciprofloxacin.

**Other bioenhancers:**

- *Ammania multiflora* 10
- *Cleome rutidosperma*/Fringed spider flower/purple cleome 34, 42
- *Eclipta prostrate*/false daizy/*bhringrag*/*kehraj* 44
- *Tinospora cordfolia*/*guduchi*/*gulvel* 43
- *Tribulus terrestris*/*gokharu* 48
- *Andrographis paniculatr*/*kalmegh* 42

- Arctium lappa/Indian berry <sup>42</sup>
- Boerhavia diffusa/ punarnava <sup>42</sup>
- Embellia ribes/vidand/vavding <sup>43</sup>
- Rubia cordifolia/manjishtha <sup>44</sup>
- Eucalyptus <sup>36</sup>
- Terpentine <sup>36</sup>
- Boswellia oil <sup>48</sup>

#### Bioenhancers from animal source:

##### Cow urine: <sup>6, 27, 45-47</sup>

As per Ayurveda, cow urine is considered as the elixir of life.

Cow urine is an antiseptic and stated as 'Sanjivani' in Ayurveda. It is most effective in treating all kinds of infections particularly those of the kidney and liver. Cow urine balances the "tridosha" (vata, pitta and kapha). Essential micronutrients are flushed out of the body after urination.

Nowadays plain cow urine is replaced with filtered cow urine, cow urine distillate, purified cow urine, cow urine fraction. Cow urine acts as a bioenhancer in drugs: rifampicin, tetracycline, ampicillin, paclitaxel, zinc, taxol, INH, clotrimazol, cynocobalamine, mercaptopurine.

##### Ghee: <sup>48</sup>

Also called as tup, ghi, ghio, neyy. cow ghee is mostly preferred in ayurveda, it is satvik in nature i.e. sattva guni. It acts as bioenhancer in many ayurvedic formulations like Brahmi ghrita, Trikutrayadi lauha.

##### Honey:<sup>48</sup>

It is known as madhu too. It is sweet food made by bees using nectar from flowers. In modern practice it is used in crystallized, pasteurized, raw, strained, filtered, ultrasonicated, creamed, dried forms, nowadays honey decoctions are also available. Used as a bioenhancer in Trikutrayadi lauha.

#### Mechanism of action:

Bioenhancers have various mechanism 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. <sup>3,4,10-12, 17</sup>
2. It inhibits gastrointestinal transit, gastric emptying time and intestinal motility. <sup>11</sup>
3. By enhancing permeability of GIT epithelial cell membrane. Example includes naiziridine, piperine, gingerol etc. <sup>4,10, 17</sup>
4. It inhibits or reduces the rate of biotransformation of drug in liver or intestine. <sup>3</sup>
5. By modifying immune system to reduce overall requirement of drug. <sup>4</sup>
6. By allowing entry into pathogen or by increasing penetration where they become persistors within macrophases such as for mycobacterium tuberculosis example: nitrile glycosides. <sup>12</sup>
7. By inhibiting ability of pathogen or tissue to reject the drug. <sup>10</sup>

8. By hindering drug metabolizing enzymes like CYP3A4, CYP1A1, CYP1B2, CYP2E1 in gut, lungs or various locations example: quarcetin, naringin. <sup>3, 4, 10, 11</sup>
  9. By stimulating gamma glutamyl transpeptidase (GGT) actively which enhance amino acid uptake. <sup>10, 11, 17</sup>
  10. By modifying signaling process between host and pathogen to increase accessability of drug to pathogen. <sup>3</sup>
  11. By enhancing binding of drug to receptors, proteins, DNA, RNA and potentiate and prolong its effect. <sup>3,12</sup>
  12. Cholagogous effect i. e. it stimulate gall bladder contraction to promote flow. <sup>10, 11, 17</sup>
  13. By restraining renal clearance by preventing glomerular filtration and active tubular secretion by inhibiting P-gp and facilitating passive tubular reabsorption. <sup>10,11, 12</sup>
  14. Bioenergetics and thermogenic property. <sup>10, 11, 17</sup>
- Mechanism of various bioenhancers are still unknown.

#### Problems / limitations / hurdles with Bioenhancers <sup>4, 10, 12</sup>

Even though drug delivery using bioenhancer reached at greater degree, not all approaches met with same success. Still few challenges have to be solved or modified which includes physicochemical character to improve long circulation in blood, drug protection, site specific targetting, crossing biological barriers, increased surface area. another challenge is development for large scale production, there is need of scale up techniques and pilot techniques for commercialisation. Scaling up challenges include low concentration of nano materials, agglomeration and chemistry processes which can be easily modified at laboratory scale.

Regulatory control as a challenge for conventional drug product. there are few standards for physicochemical and pharmacokinetic properties by US-FDA and EMEA in case of products using bioenhancer yet no any standards are set, so regulatory authorities should have take initiative to set standards for such product.

#### Future Scope:

Research on Bioenhancer is going on for Pain Management, Stress, Obesity, Anticancer etc. Unexplored areas of Ayurvedic and other traditional systems of medicines could be an additional area where new breakthroughs can be expected. Work on all categories of drug can be carried out. Studies to know exact mechanism of bioenhancer could be a next step. Like conventional dosage forms, modern dosage forms can be prepared using *Yogvahi*. In case of products using bioenhancer yet no any standards are set by regulatory authorities, so such initiative should be expected to take to set the standards for such products.

#### III. CONCLUSION

Ayurveda has long lasting effect. There is need of using modern technology by scientifically linking primary understandings of Ayurveda, these concepts should be constructed in scientific language to put on a map of modern health care. "Yogvahi" concept of Ayurveda relates to the "Bioenhancer" terminology of modern medicine.

Bioenhancers are interface between modern medicines and ancient systems which gives best examples of both modern and ancient systems equally in theory and practice.

It could be explored further to co-relate its relevancy/applicability in several unexplored areas in modern medicines.

In developing countries like India, where the economic condition for the use of modern medicine are unaffordable, there such systematic innovative aspects to decrease costs could be a breakthrough to improvise health practices.

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