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REVIEWS ON: NATURAL BIO ENHANCER YOGVAHI MEDICATIONS FOR TREATING OSMF

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ABSTRACT: “Bioenhancing activity” is considered as a revolutionary concept that is being researched and tested in various modern medicines, but its roots, in general, has been obtained from a classical system of medicine called “Ayurveda”. In Ayurveda, the concepts which promote the mechanism of bio enhancing activity are of: Yogavahi, Anupana, Bhaishajya kala, Rasayana, Various Yoga (Formulations), Purana Aushadhies, Penetration enhancers, Action augmenting drugs, Bhavana, and Process of Samshodhana. In this article, an attempt has been made to explain the concepts and mechanism of Yogavahi, and to throw light on the various drugs and processes mentioned in Ayurveda with Yogavahi property. A precancerous disorder of the mouth, oral submucous fibrosis (OSMF), is typically characterised by inflammation and increasing fibrosis in the submucous region, causing tongue protrusion, intense burning sensation, trismus, and difficulty opening the mouth. It is widely acknowledged that OSMF is an Indian disease that has the greatest incidence of oral cancer. This research aims to shed light on the comprehensive use of Yogavahi (ayurvedic) medications for treating OSMF.

INTRODUCTION: Bioenhancers or Bio potentiators are those agents which do not show any pharmacological action of their own at the therapeutic dose used, instead, they when combined with the active drug, lead to the potentiation of the pharmacological activity of the Drug. Today, it is of great importance and interest to improve the bioavailability of medications that are poorly bioavailable, costly, besides dangerous. There are numerous factors that can contribute to inadequate absorption of medication through the mouth.

These factors include insufficient dissolution and solubility in water, limited permeability across the intestinal barrier, degradation of the drug in gastrointestinal and intestinal fluids, and metabolism in both the intestines and liver¹. The main drug and co-administered drug are used to maximize overall bioavailability and bioefficiency, but this agent is not the main drug. Increasing the level of drug in the bloodstream for drug action is achieved by maximizing bioavailability.

While increased bio-efficiency refers to increasing the potency of the drug. Bioenhancers work through variety of mechanisms, including increasing the absorption of drugs from the digestive tract, reducing the rate at which drugs are metabolized by the liver, and altering the immune system to a point where the total drug requirement is significantly reduced.

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The term "Bioenhancer" was first used in 1929 by German scientist Bose in his textbook "Pharmacographia Indica", Bioenhancers as a newly introduced in clinical science become first scientifically set up in 1979, by Indian scientists Dr C. okay. Atal and his research crew at RRL Jammu, once they discovered and tested Piperine as the arena's first bioenhancer²⁻⁵.

"YOGVAHI" refers to an agent that, in addition to serving as a catalyst, can also function as a "Carrier" for the macromolecules of active substances, delivering them to the site of action. Yogvahi properties can reduce process side effects, avoid parenteral drug delivery routes, and improve drug absorption, tissue distribution, and efficacy. The most crucial component of any polyherbal Ayurvedic formulations is synergism, which can be achieved through the use of bioenhancer Yogvahi dravyas.

Ayurvedic practitioners most frequently use Pippali (Piper longum) and Maricha (Piper nigrum) as examples of Yogavahitwa. However, the following

are some more examples: Vata Dosha, Madhu, Ghrita, Paradha, Bhasmas, Guggulu, and Ksheerapaka²⁻³.

Oral submucous fibrosis (OSMF) is a precancerous disorder that affects the entire mouth cavity and occasionally the pharynx. It produces inflammation and increasing fibrosis, which stiffens the oral mucosa, causes jaw muscle spasms, and makes it difficult to eat. A doctor by the name of Schwartz described it as atropia idiopathia mucosae or is in 1952⁶⁻⁷.

It is also known as juxta epithelial fibrosis of the palate and pillars, sclerosing stomatitis, and idiopathic scleroderma of the mouth. Chronic illnesses induce inflammation in the juxta epithelium, which is subsequently accompanied by fibroblastic alterations in the lamina propria and deeper connective tissue. The condition is characterised by the persistent expansion of a collagen band in the cheeks, which limits the ability to move the tongue freely, making it difficult to eat and speak⁸⁻⁹.

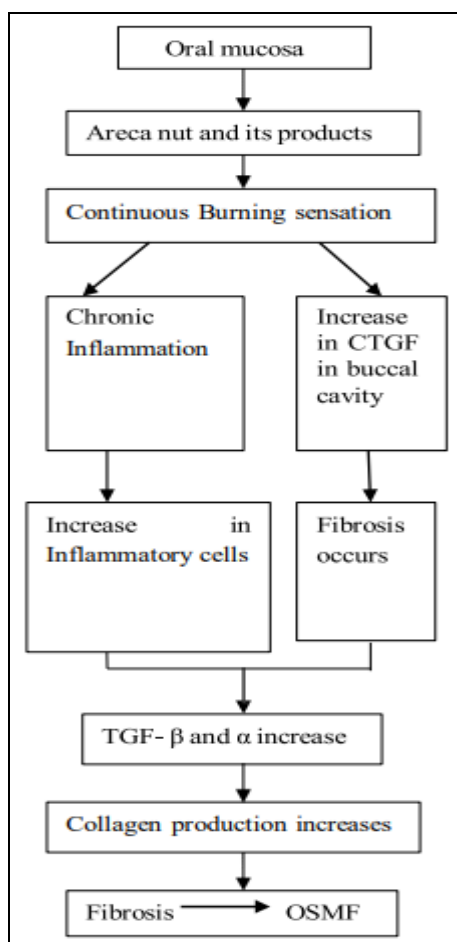


FIG. 1: FLOW DIAGRAM FOR PATHOGENESIS OF CONSUMPTION OF ARECA NUT AND VARIOUS PRODUCT

The indications of OSMF included as:

- ❖ One of the signs of OSMF was burning and blanching of the oral mucosa.
- ❖ Moderate upper bound on oral opening.
- ❖ Ovula with a bud form or reduced size.
- ❖ Depapillated tongue and oral ulcers.
- ❖ The soft palate develops a blister or marble-like appearance, and the oral mucosa becomes inflamed.
- ❖ A decrease in tongue mobility and soft palate.
- ❖ Breathlessness and excessive salivation¹⁰⁻¹².

For OSMF, a range of non-surgical and surgical options are available. Treatment with Ayurveda is one of them¹³.

Now we can discuss about Yogavahi-The capacity or aptitude to transport something to a remote location and make it available at the location of its utilisation or A material that can improve the characteristics and efficacy of the main medication; a catalytic agent that transports the therapeutic qualities of herbs into the body's tissues or the seven dhatus; or an agent that functions as a vehicle to deliver the necessary material to its intended location. This is also how the bioenhancer's mechanism functions. Thus, our ancient Ayurvedic texts refer to the idea of the Yogavahi characteristic as a way to increase bioavailability¹⁴.

The most widely used Ayurvedic Medications and that have the Yogavahi Property are:

A. Honey (Madhu): Honey is mentioned as the best Yogavahi in Ayurvedic literature¹⁵. It is Madhura in Rasa with Kashaya Anurasa; it balances pitta and kapha doshas, is hot in potency, and is easily digested. Honey is regarded by Acharya Susruta as Sreshta Yogavahi⁷, a material with the ability to pierce even the deepest tissue.

This means that it works wonders as a co-drink for a lot of Ayurvedic medications, acting as a catalyst and facilitating the quick delivery of the medication to the intended location without affecting its characteristics. The fact that Acharya Caraka listed it as one of the Pathya dravyas attests to the medicinal value of honey. It is the strongest and most effective among since it comes from a variety of plants and flower varieties.

It is most powerful of all the Yogavahi dravyas. It is known as "Param Yogavahi" since administering madhu in combination with different formulations improves their therapeutic properties, particularly for treating kapha problems¹⁶.

Pharmacology Activity¹⁷:

TABLE 1: PHARMACOLOGICAL ACTIVITY OF HONEY

Sr. no.	Pharmacological Activity
1.	Buck wheat honey increases serum antioxidant capacity in humans
2.	Anti-hyperglycaemic activity
3.	Antimicrobial and Anti-inflammatory activity
4.	Wound Healing
5.	Honey and gastric ulcers
6.	Antimicrobial Activity
7.	Analgesic and anti-inflammatory effects of honey
8.	Anti-viral activity
9.	Anti-allergic activity

Here are a few Ayurvedic recipes that use Honey as a Catalyst:

- ❖ Swasakuttara Rasa
- ❖ Anadhabhairavi Rasa
- ❖ Vasanthamalathi Rasa
- ❖ Hinguleshwara Rasa
- ❖ Muktha Pishti
- ❖ Talisadhi Choorna
- ❖ Sithopaladhi Choorna
- ❖ Triphala Choorna
- ❖ Trikatu Choorna
- ❖ Haridra Choorna
- ❖ Balachathurbhadra Choorna
- ❖ Abhraka Bhasma
- ❖ Vasanthakusumakara rasa
- ❖ Sanjivani Vati
- ❖ Arogyavardhini vati
- ❖ Shanka vati
- ❖ Navayasa loha
- ❖ Yogendra rasa

Pippali and Maricha: Alkaloid compound piperin is widely distributed in Maricha (*Piper nigrum*) and Pippali (*Piper longum*). Since the beginning of

time, it is regarded as the first and most widely utilised bioenhancer. It has been documented to improve the bioavailability of a range of medications and nutraceuticals by either speeding up absorption or slowing down drug metabolism. Numerous studies have been conducted up to this point that demonstrate the significant role that piperin plays in both allopathic and ayurvedic medicine as a bio enhancer¹⁷.

Ghrita: Since ancient times, ghee and Ayurveda have had a very intimate relationship. Ghee is regarded as an ideal foundation for making Ayurvedic medications due to its unique capacity to quickly penetrate all organs and tissues, aiding in the delivery of the medication to its intended location. Due to its "Yogavahi" properties, ghee is used as a medium for a variety of medicines and infusions. It functions in numerous Ayurvedic formulations as a bioenhancer. When compared to other cooking oils, ghee reduces the activity of the enzymes that cause the liver's carcinogens to become active. Ghee lowers the risk of cancer by increasing the body's detoxification of carcinogens. Because ghee has an innate Prabhava that allows it to absorb the therapeutic benefits of other plants without losing its own, it is particularly helpful in this regard. For example, Ghee can absorb the amla virtues of another herb without losing its sweet attributes. Particular of the Ayurvedic formulations where Ghrita is acting as a catalyst¹⁸⁻¹⁹.

TABLE 2: AYURVEDIC FORMULATIONS WHERE GHRITA IS ACTING AS A CATALYST

Sr. no.	Ayurvedic formulations where Ghrita is acting as a catalyst
1.	Talisadhi Choorna
2.	Sitopaladhi Choorna
3.	Brahmi Ghrita
4.	Hinguashtakam Choorna
5.	Navayasa Loha
6.	Vasa Avaleha
7.	Kalyanaka Ghrita
8.	Mahakalyanaka Ghrita
9.	SaraswathaGhrita
10.	Mahapaishachika Ghrita
11.	Panchagavya Ghrita

Parada: Given that Parada (Mercury) is a divine metal, it is considered auspicious. In mythology, it is identified with Lord Shiva's Veerya. Shadrassa, Snigdha, Sara, and Guru guna are present in Parada, together with a unique quality (Prabhava) known as "Yogavahitwa"¹⁰.

It follows that Parada can enhance any substance it is combined with's therapeutic qualities. The most common application of this metal is in Ayurvedic medicine, particularly in Rasayogas where it is utilised as Bhasma. While all formulations containing Parada demonstrate the Yogavahitwa quality, Rasa Sindur stands out due to its detailed description of many indications and their corresponding Anupanas. For instance, Rasa sindur is reported to increase the therapeutic efficacy of Khadhira Kashaya in Kushta Roga when taken with it. Rasa Sindoor's Yogavahitwa skill is the reason behind this²⁰.

Selected of the Rasa Preparations which are Yogavahi in Nature:

- ❖ Sutashekara Rasa
- ❖ Panchavakta Rasa
- ❖ Tarakeshwara Rasa
- ❖ Jwaramurari Rasa
- ❖ Hingullotha parada
- ❖ Rasa Sindur

Guggulu: The term "guggulu" describes the Oleo-Gum resin that is extracted by making an incision in the Guggulu tree's (*Commiphora mukul*) bark. Guggulu is known as Yogavahi because it has the ability to reach even the smallest areas of the body and eliminate deeply ingrained poisons from the body's tissues. Rarely consumed on its own, this herb holds significant value in Ayurvedic medicine. Guggulu is used in many Ayurvedic formulations called Guggulu Kalpanas, where it enhances the other medications in the formulation without diminishing its efficacy and has significant therapeutic effects. Therefore, this medication is administered for a variety of illnesses with distinct Anupanas. These Guggulu compounds are made by combining purified Guggulu with a variety of other useful plants in a synergistic way. Acharya Susruta has provided some excellent information regarding Guggulu²¹. It was recommended that Guggulu be taken internally in liquid, semi-liquid, or semi-solid form. However, the solid dose forms offer additional benefits. Other than the remaining internal forms, Guggulu was later frequently employed in Vati form. This occurs as a result of

the drug's binding and yogavahi properties, which boost the effectiveness of different formulations.

Some of the Important Guggulu Formulations are:

TABLE 3: GUGGULU FORMULATIONS

Name of Guggulu	Formulations
Yogaraja Guggulu	Vataroga
Kaisora Guggulu	Vata Rakta
Triphala Guggulu	Vrana, Sthoulya Kanchanara Guggulu Gandamala Gokshuradi Guggulu Prameha
Simhanada Guggulu	Amavata
Laksha Guggulu	Bhagna Saptavimsati Guggulu Bhagandhara

Vata Dosh: Vata is extremely significant because of its excellent Yogavahitwa quality. The Yogavahitwa notion of Vata dosha has been briefly elucidated by Acharya Sharangadhara.

The following are key Ayurvedic Formulations where the Yogavahitwa of Vata dosha is considered the Most Important:

- ❖ Dosha Prasara
- ❖ Koshta Gati
- ❖ Shaka Gati
- ❖ Ashayapakarsha Gati

Ksheera Paka: Cow's milk is the primary ingredient or medium in Ksheera Paka, a sort of pharmaceutical preparation, as milk may improve the qualities of the medications put to it. All of the active ingredients in milk are removed according to their polarity due to the presence of both polar and non-polar solvents, namely water and fat. The primary goal of this Kalpana is to lessen the Teekshnata of the medications that are added to it while also delivering the therapeutic benefits of Samskarita and Ksheera.

This makes it extremely helpful in situations where direct prescriptions for milk products are not possible. The solubility of fat and protein in milk is enhanced by raising its temperature, which facilitates the extraction of active ingredients that are significant to medicine and are readily absorbed through bodily membranes.

Few of the Ksheera Paka Preparations used are:

- ✓ Rasona Ksheera Paka

- ✓ Shunti Ksheera Paka
- ✓ Arjuna Ksheera Paka
- ✓ Guduchi Ksheera Paka
- ✓ Pippali Ksheera Paka
- ✓ Haridra Ksheera Paka ²¹⁻²²

Justification for Improving Bioavailability: "The phenomena of improving the overall occurrence of any chemical substance in the biological fluid and systemic circulation, as well as secondary chemicals responsible for the increase in plasma drug concentration of the major component, are referred to as biopotential or bioenhancement."

Bioenhancers are employed in diverse techniques to enhance bioavailability. Examples of particular tactics include P-glycoprotein inhibitors, prodrugs, permeability boosters, micronization, and formulations of pharmaceutical formulations with prolonged and sustained release, such as liposomes and emulsions (P-GP) ²³.

Bioenhancers Possess the Subsequent Characteristics ^{24, 25}:

- ❖ Its nature need to be nontoxic.
- ❖ It should be easy to put into words.
- ❖ When taken with the medication, it ought to have an impact at a very low concentration.
- ❖ It ought to boost the medication's action and absorption.
- ❖ Adherence is easy.
- ❖ Acceptance is easy due to the inexpensive cost.
- ❖ Simple to get to.
- ❖ It needs to be allergy-free and non-irritating.
- ❖ It must be responsive and steady in its environment.

The benefits of bioenhancer:

- ❖ The dosage of the medication is lowered and the likelihood of drug resistance is reduced when a bioenhancer is used in conjunction with a medication.
- ❖ The reduced dosage will result in a decrease in toxicity and unfavourable medication reactions or side effects.

- ❖ This is especially true when it comes to anticancer drugs like Taxol.
- ❖ The drug's efficacy has enhanced as a result of improved bioavailability.
- ❖ Drugs can reduce intra- and inter-individual variability as their bioavailability increases ²⁶.

The Drawbacks of the Bioenhancer:

- ❖ Several obstacles facing the development of new bioenhancers, including.
- ❖ Improving the characteristics of medication formulations, such as site-specific targeting, drug dissolution protection, functional surface area, blood circulation, and biological barrier passage.
- ❖ It's challenging to research and develop bioenhancer for large-scale production. For eventual commercialization, laboratory or pilot technologies must always be scaled up.
- ❖ Low nanoparticle concentrations, aggregation, and the thin-film chemical procedure are scaling-up issues; nanoparticle modification is simpler in the thin-film laboratory.
- ❖ Newer bioenhancers need to have their phytochemical and phytokinetic properties regulated ²⁷.

Using a natural bioenhancer has a number of advantages, some of which are listed in **Fig. 2** ²⁶.

Bioenhancers Based on Mechanism of Action ²⁸:

TABLE 4: BIOENHANCERS BASED ON MECHANISM OF ACTION

Inhibitors of P-gp efflux pumps	Example: <i>Cuminum cyminum</i> (Black cumin), Carumcarvi (caraway), Genistein, Sinomenine, Naringin, Quercetin
Suppressors of CYP-450 enzyme and its isozymes	Example: Naringin, gallic acid, and its ester, quercetin
Regulators of GIT function to facilitate better absorption	Example: Niaosidin (drumstick pods), <i>Zingiber officinale</i> (ginger), Aloe vera (Aloe), and glycyrrhizin (licorice)

The way that Bioenhancers Work: Herbal bioenhancers function in multiple ways. The mechanisms of action of various bioenhancers can be the same or different. Nutritional bioenhancers enhance absorption by acting on the gastrointestinal system. Antimicrobial bioenhancers mainly affect how drugs are metabolised ²⁹.

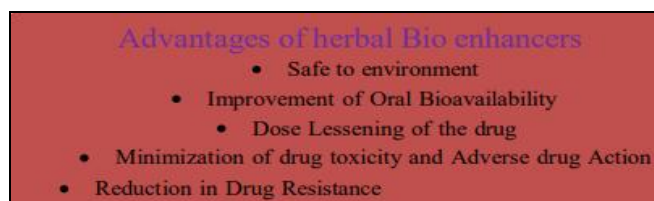


FIG. 2: ADVANTAGES OF HERBAL BIOENHANCERS

Classification of Bioenhancers:

Bioenhancers are Divided according to where they came from ^{15,16}:

- ❖ Bioenhancers sourced from vegetation these bioenhancers are composed of various plant components. It is believed that secondary metabolites from numerous aromatic and medicinal plants are a rich source of bioenhancers.
- ❖ Bioenhancers sourced from non-plant materials the second category consists of bioenhancers that come from non-herbal sources. To get and synthesise these bioenhancers, non-herbal and synthetic chemical substances can be employed.
- ❖ Plant-based bioenhancers
- ❖ Bioenhancer from Capmul Source Capmul is made *via* glycerolysis of particular fats and oils and esterification of glycerin with particular fatty acids (mono-, di-, and triglyceride) ²⁷.

Example-Medication Ceftriaxone 70 (the lipophilic nature of capmul contributes to the improved solubility of Ceftriaxone 70). Urine distillate from cows Compared to cow pee, cow urine distillate is a more effective bioenhancer ²⁸.

The primary methods via which various bioenhancers raise the medicinal component's bioavailability are as follows ³⁰:

- ❖ The blood supply to the GIT tract is restricted, which improves the absorption of medications taken orally.

- ❖ It is possible to alter active transporters at many locations, such as glycoprotein (p GP), the efflux pumps that remove medications from the body and stop them from reaching their target site. Inhibiting drug metabolism enzymes in the liver, stomach, lungs, and other locations, including CYP3A4, CYP1A1, CYP1B2, and CYP2E1, is how bioenhancer functions in these circumstances. Additionally, this will aid in the first-pass effect of medications.
- ❖ Reducing renal clearance, which lowers passive tubular reabsorption, prevents glomerular filtration, and stops active tubular secretion. Sometimes biliary transit can be obstructed by inhibiting the UDP glucuronosyl transferase enzyme, which conjugates and inactivates the medication.

TABLE 5: BIOENHANCER, DRUG WITH BIOENHANCERS WITH MECHANISM

Sr. no.	Bioenhancer	Biological origin	Class	Drug with bioenhancers	Mechanism	Ref.
1	Piperine Part used- Seeds	Piperlongum and Piper nigrum Family- Piperaceae	Amid alkaloid	Nevirapine, Rifampicin, Propranolol, Nifedipine, Ciprofloxacin	Piperine's methylenedioxyphenyl ring helps to Inhibit drug-Metabolising Enzymes such as CYP450 and UDP Glucuronyl Transferase. P-gp is Also inhibited, Causing drug Efflux from Enterocytes	[31]
2	Curcumin Part used- Rhizomes	<i>Curcuma longa</i> Linn Family- Zingiberaceae	Curcuminoids	Celiprolol, Midazolam	Curcumin suppresses drug-metabolising enzymes (CYP3A4) in the liver, causing changes in the Drug transporter P-Glycoprotein, Which raises the Cmax and AUC of Celiprolol and Midazolam in rats	[32-34]
3	Quercetin	This flavonoid May be found in A variety of fruits (Apples, citrus Fruits such red grapes, raspberries, and cranberries), green leafy vegetables, and black and green tea.	Favonoid	Diltiazem, Digoxin, Epigallocatechin gallate	It inhibits the p-Glycoprotein efflux Pump and the Metabolising Enzyme CYP3A4 In the intestinal Mucosa and restrains the metabolizing enzyme CYP3A4	[35]
4	Ginger Part used-Whole Part	Zingiber <i>Officinale roscoe</i> , Zingiberaceae family	Saponins, flavo-noids, alkaloids	Antibiotics like Azithromycin, Erythromycin, Cephalexin, Cefadroxil, Amoxicillin, and Cloxacillin	The saponins, flavonoids, and Alkaloids in ginger have a Powerful effect On the GIT Mucosal Membrane	[36]

5	Indian aloe Part used- Leaves	Aloebarbadensis Mill.,	Liliopsida	Indianaloe(Leaves)	Aids absorption by Modulating Gastrointestinal Function Aloe, when Combined with Vitamins, slows down and Prolongs Absorption	[37]
6	Caraway Part used- Seeds	Carumcarvi Linn., Family- Apiaceae	Flavonoid	Antibiotics, antifungal, antiviral, and anticancer medications, Anti- TB medications including Rifampicin, Pyrazinamide, and Isoniazid have Therapeutic efficacy	Because of new flavonoids, rifampicin’s peak concentration (Cmax) and area Under the curve (AUC) are Increased	[38, 39]
7	Capsaicin Part used- Fruit	<i>Capsicum annum</i> Linn., Family- Sola-naceae	Capsaicinoid	Theophylline	Capsicum Enhances the AUC of the Medicines by increasing their absorption	[40]

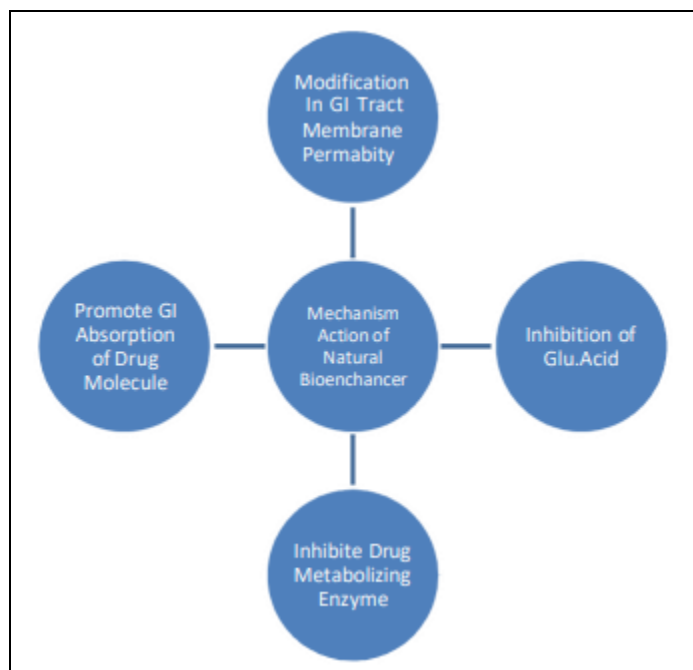


FIG. 3: MECHANISM OF DIFFERENT NATURAL BIOENHANCERS ⁴¹

TABLE 6: LIPOSOMAL FORMULATION CONTAINING NATURAL BIOENHANCER

Liposomal formulation	Bioenhancer	Application	Preparation method	Biological activity	Mode of administration	Ref.
Liposome of querce- tin- epigallocatechin gallate	Quercetin	Lowered dose, increased penetra- tionthrough blood– brain barrier	Reverse Evaporation method	Anti-oxidant Anti-cancer	Intranasal	[42]

Liposome of Curcumin piperine	Piperine	Hightrap efficiency with long circulation	Ethanol injection Technique	Anti-inflammatory, anti-virus, and anti-tumour	<i>In-vitro</i>	[43]
Liposome of Artemisia arborescence	Artemisia arborescenc (Artemisia itself acts as a bioenhancer)	Essential oils maybe directed to specific cells	Sonication and the film process	Antiherpetive	<i>In-vitro</i>	[44]
Liposome of garlic-amphotericin	Garlic	Lead to increased efficiency	Hydration of thin films	Anti-fungal	Topical	[45]
Liposome of encapsulated silymarin	Silymarin (Silymarin itself acts as a bioenhancer)	Enhance bioavailability	Technique of reverse evaporation	Hepatoprotective	Buccal	[46]

TABLE 7: NANOPARTICLE FORMULATION CONTAINING NATURAL BIOENHANCER

Nanoparticle formulation	Bioenhancer	Application	Preparation method	Biological activity	Mode of administration	Ref
Nanocapsules of artemisinin	Artemisinin	Long-term medication release	Layer-by-layer technique	Anticancer	<i>In-vitro</i>	[47]
Nisoldipine piperine nanoparticles	Piperine	Improve bioavailability	Precipitation method	Calcium channel blocker	Oral	[48]
Isradipine-rutin nanoparticles	Rutin	Enhanced systemic bioavailability	Homogenization by the ultrasonication method	Hypertension	Oral	[49]
Amphotericin B-piperine nanoparticles	Piperine	Enhanced bioavailability	Solvent evaporation method	Antileishmanial activity	Oral	[50]
Paclitaxel-piperine, quercetin nanoparticles	Piperine, Quercetin	In comparison with free paclitaxel, it has greater solubility and bioavailability	Solvent evaporation method	Anticancer	Oral	[51]

TABLE 8: TRANSFEROSOME FORMULATION CONTAINING NATURAL BIOENHANCER

Transfer some Formulation	Bioenhancer	Application	Preparation Method	Biological activity	Mode of administration	Ref
Colchicine-Cyclodextrin Transferosome	Colchicine	Increase skin penetration	Thin-film hydration method	Acute gout	<i>In-vitro</i>	[52]
Capsaicin-mitoxantrone hydrochloride Transferosome	Capsaicin	Increase skin penetration	Conventional Thin film hydration method	Antiarthritic	Topical	[53]

TABLE 9: MICROSPHERES FORMULATION CONTAINING NATURAL BIOENHANCER

Microspheres formulation	Bioenhancer	Application	Preparation Method	Biological activity	Mode of administration	Ref
Isoniazid-piperine microspheres	Piperine	Sustained Release formulation	Double emulsification method & complex coacervation	Tuberculosis	<i>In-vitro</i>	[54]

Acyclovir-piperine microspheres	Piperine	To boost oral bio-availability, place the medicine in the upper gastrointestinal area	method Emulsification solvent evaporation method	Active against HSV-1 and HSV-2 herpes simplex viruses	Oral	[55]
Famotidine-quercetin microspheres	Quercetin	Alternative for treating peptic ulcer	Ionotropic gelation method	Peptic ulcer	Oral	[56]

Optimising bioavailability is the ultimate goal when using herbal medications with Yogavahi properties because it directly affects plasma concentrations, which raises therapeutic efficacy. Additionally, increasing bioavailability can lower the cost of expensive medications and lessen their adverse effects by lowering the dosage needed. The above-mentioned drugs and processes, including Pippali (*Piper longum*), Maricha (*Piper nigrum*), Madhu, Ghrita, Paradha, Bhasmas, Guggulu, Vata Dosha, and Ksheerapaka, possess the Yogavahitwa property. This led to the development of advanced formulations under a variety of categories, including Kashaya, Vati, Asava, Arishta, Avaleha, Paka, Khand, Bhasma, Pishti, and so on 57.

Nowadays, oral cancer ranks as the fifth most common type of cancer detected in humans. Oral sub mucous fibrosis (OSF) is a disease caused by a chronic change in fibro-elasticity, characterized by a burning sensation in the oral cavity, blanching and stiffening of the oral mucosa and oro-pharynx leading to trismus and inability to open the mouth. Oral cancer is a major problem in India, accounting for 50-70% of all cancers diagnosed, compared to 2-3% in the UK and USA¹. The number of afflicted locations and the rate at which the lesions grow determine the symptoms and indicators. The majority of people who have it are Asians, including Indians. Once the illness has taken hold, there is no recovery and no reliable therapy. It is regarded as an early stage of oral cancer, with a reported risk of 2.3–7.6% for malignant transformation⁵⁸.

DISCUSSION: In the world of medicine, bioenhancers are extremely helpful since they reduce costs, toxicity, and other negative effects. They have a broad impact on many drug classes and are inexpensive, safe, and efficient. Numerous studies in the scientific community have demonstrated that co-administration of bioenhancers with primary medications

significantly improves their bioavailability. After compounds like piperin and quercetin were developed and isolated, science made significant progress in understanding bioenhancers. Many studies have been conducted that shown how adding different herbs with bioenhancing properties improved the bioavailability of many medications

In Ayurveda, the idea of a bioenhancer is known as yogavahi. The capacity to transport objects to far-off locations and make them available where they are needed is known as yogavahitwa. When compared to current drug forms that have greater bioavailability, decreased bioavailability has become a big issue for all Ayurvedic Pharmaceuticals and formulations. This is where the aforementioned Ayurvedic bioenhancer comes in to play a major part in improving the bioavailability of the main drugs. In Ayurveda, some common examples of Yogavahitwa medications are Maricha (*Piper nigrum*) and Pippali (*Piper longum*). The others are, on the other hand, Vata Dosha, Madhu, Ghrita, Paradha, Bhasmas, Guggulu, and Ksheerapaka.

All of the pertinent data regarding the Yogavahitwa properties of these medications demonstrates how the conventional understanding of these Ayurvedic medications demonstrates their bioenhancing properties. A precursor to cancer that affects the oral mucosa is called oral submucous fibrosis (OSF). Tobacco, areca nut, and betel quid consumption are the primary causes of OSF. It is a social norm among India's rural and impoverished populations to consume areca nuts with or without tobacco. In cases of oral submucous fibrosis (OSF), Ayurvedic treatments such as triphala, tulsi, haldi, and ghritkumari can be readily obtained and used.

Future Prospectus: Bioenhancers has proven to be extremely groundbreaking in today's environment. Both the danger of medication resistance and the dosage of bioenhancers are decreased.

The toxicity of the medications is decreased as a result of the lower dosage; this is particularly true for cancer medications like Taxol.

There are advantages for the environment as well. One of the biggest and slowest growing plants in the world, the Pacific yew, is used to make the medication Taxol, which is used to treat ovarian and prostate cancer.

Researchers are currently looking into approaches to improve therapeutic accessibility for a larger group of individuals, including supporting the country financially, and reduce drug dosages and treatment expenses. The yogavahi bioenhancing treating *Oralsubmucous fibrosis* (OSMF) phenomenon has several positive side effects that help society.

CONCLUSION: The discovery of the novel idea known as "yogavahi bioenhancing activity" was founded in the Ayurvedic medical system. Many of the commercially successful medicine combinations were created by fusing modern research techniques with the natural wisdom of Ayurveda. The vast array of polyherbal medicine combinations used in Ayurveda is a science whose medicinal value stems from their synergistic effect. The medications in these polyherbal combinations' bioenhancing abilities are what ultimately causes this. In addition to Yogavahi, the following other elements can increase bioavailability: Anupana, Rasayana, Bhaishajya kala, Purana Aushadhies, Penetrating enhancers, Samshodhana procedure, and Bhavana.

Oral submucous fibrosis (OSMF) is a precancerous disease that progresses over time. Ayurvedic medicine has been demonstrated to be a beneficial alternative therapy for treating OSMF, despite the fact that there are ineffective non-surgical and surgical therapies available. Ayurvedic treatment also ensures that diseases will be cured without harmful drug side effects. It is believed that compared to other surgical and non-surgical methods, ayurvedic treatment for OSMF yields better results.

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