

## Study on the bioavailability enhancers used in Unani formulations in the light of recent pharmacological advances: A review

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### Abstract

Since ancient times herbal formulations have been used with promising efficacy. However, at present, they suffer from poor bioavailability due to poor absorption resulting in poor efficacy. This is mainly due to the role of supportive ingredients being either being ignored or neglected. This study is focused on the bio-enhancing property of the supportive ingredients. Unani classical texts, Pharmacopoeias and research articles were thoroughly reviewed with regard to Bioenhancers used in formulations commonly used in Unani. The main objective of this review is to understand the concept of bioavailability, identify supportive ingredients (*Mufrad Dawa*) to enhance the bioavailability and to promote the use of authentic supportive ingredients in compound medicines. It was found that the supportive ingredients in combination with an active drug lead to the potentiation of the main therapeutic moiety of the drug. A *Murakkab Dawa* (compound medicines) contain supportive ingredients which improve the bioavailability of the active ingredient thus, resulting in promising efficacy. This review explores the *Mufrad Dawa* in compound formulations in various Pharmacopoeias for ingredients like *Fil fil e siyah*, *Fil fil e daraz*, *Zanjabeel* with bio potentiation action. These drugs are *Garam vo Khushk* (hot and dry) in temperament with characteristic tastes like pungent, sour and salty attributed with heating property and possess actions of *Muqawwi e Hazim* (digestive tonic), *Muqawwi e Medha* (stomachic), *Kasirriyah* (carminative) etc; These supportive ingredients act collectively and synergistically to overcome the poor absorption of the active therapeutic moieties to increase the active moiety in blood enhancing the therapeutic effects

which helps in minimizing the doses, side effects and shorten the period of treatment.

**Keywords:** Bio-enhancers, *Murakkab Dawa*, *Muqawwi e Medha*, *Muqawwi e Hazim*. Supportive Ingredients.

### Introduction

Indigenous Systems of Medicine have been playing a major role in preventing and effecting cure for a number of diseases since ancient times. These systems of medicine possess a large number of herbal medicinal products with promising efficacy. As a result, the use of herbal medicinal products has increased tremendously over the last few decades. However, many of these herbal medicinal products do not show promising effect as expected mainly due to poor absorption resulting in poor bioavailability of their active components<sup>1,2,5</sup>.

Bioavailability is the rate and extent at which the active drug ingredient or therapeutic moiety is absorbed from the drug product and becomes available at the site of action<sup>3,4</sup>. In general, the drugs administered orally are poorly bioavailable as they readily undergo first pass metabolism. Therefore, modern medical sciences have developed various strategies and introduced a wide range of dosage forms to improve the bioavailability of poorly absorbed drugs. This shows that the bioavailability of a drug is principally determined by the property of the dosage form augmented by technology<sup>5,7</sup>.

In the Unani System of Medicine, the property of the *Murakkab Dawa* or dosage form mainly depends on the ingredients it consists of. A prescription of a *Murakkab Dawa* (compound medicine) usually incorporates several supportive

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views to improve the bioavailability of the active ingredient or therapeutic moiety of the formulation when they are given in the form of *Murakkab Dawa*. As a result, it is believed that the property of a Compound Medicine or the combined effect of its supportive ingredients play an important role in the absorption of the principal drug/s after the administration and thus increasing the active moiety or moieties of the *Murakkab Dawa*. In this context, the Unani System of Medicine possesses a treasure of empirically designed and developed drug combinations (*Murakkab Dawa*) that provide amazing therapeutic effects.

However, in the recent past, the substitution of supportive ingredients with low quality drugs or preparing compound medicines without supportive ingredients has become common practice. This has become a major impediment in producing effective compound medicines and thus, the compound medicines lose their effectiveness<sup>1,5,8</sup>.

Consequently, it is essential to identify the supportive ingredients that act as bioenhancer/s in *Murakkab Dawa* and how those ingredients contribute to absorption and higher bioavailability of the active moiety or moieties in order to accomplish valuable insights into the fascinating role of the supportive ingredients incorporated into those *Murakkab Dawa*.

Therefore, this study was conducted to understand the traditional (Unani / Ayurveda) wisdom of substances in enhancing bioavailability through modern phenomena. And the specific objectives of this study were, to explore the concepts of bioavailability to achieve better therapeutic responses in Unani Compound medicines, to identify effective ingredients (*Mufrad Dawa*) used to enhance the bioavailability and to promote the use of authentic supportive ingredients in compound medicines.

#### ***Unani concept on Bioenhancers used in compound medicines (Murakkab Dawa)***

In the Unani system of medicine, dosage forms have been designed to contain one or more herbs (ingredients) in specified quantities to provide intended benefits meant to treat, mitigate diseases of

human beings and or to alter the physiological function of the body. Further, personalized medicines are prepared or designed for individual patients in terms of the Unani concept. Therefore, *Murakkab Dawa* developed by ancient *Hakeems* seems to have been prepared according to the Unani concept in order to produce surprising results.

The effectiveness of a compound medicine mainly depends not only on the main ingredients but also on the supportive ingredients incorporated in them<sup>2,6,7</sup>. Further, supportive ingredients minimize the side effects of medicines and increase the therapeutic efficacy of medicines. Therefore, it is apparent that supportive ingredients play a major and important role to make compound medicine more effective.

*Murakkab Dawa* (compound medicines) used in Unani system of medicine incorporate many supportive ingredients which act as bio-enhancers that determine the bioavailability of drugs. As a result, the bioavailability and therapeutic efficacy of *Murakkab Dawa* are still high due to the incorporated drugs or substances in them. These intrinsic Bio enhancers have been used in *Murakkab Dawa* since time immemorial. Meanwhile, in certain occasions, medicines are administered with a suitable vehicle with a view to increasing the effectiveness of the medicines through smooth proper transport of the medicine to the site of action<sup>6</sup>.

A prescription of a *Murakkab Dawa* usually consists, in addition to main ingredient/s, one or more ingredients to aid absorption and deliver to the site of action. Therefore, the drugs that enhance the function of the stomach function to optimal level through their inbuilt properties are widely found in the Unani formulation (*Murakkab Dawa*). According to the Unani system of medicine, the drugs that possess the actions of *Muqawwi e Meda* (stomach tonic) strengthen and improve the function of the stomach.

They are identified as *Advia e Khareef* (pungent taste drugs), *Advia e Murriya* (bitter drugs) and *Advia e Khusbudar* (fragrant drugs). *Advia e Khareef* increases the power of digestion and absorption by strengthening the stomach through

their *Garami* or Hot properties. *Advia Murriya* act as bitter tonic and improve the stomach function through their bitterness and *Advia e Khusbudar* give pleasant odour and act as gastric tonic. In addition, *Muqawwi e Jiger* (liver tonic) drugs strengthen and correct the functions of the liver. These functions are performed by liver through *Quwwat e Hazima* (power of digestion), *Quwwat e Jaziba* (power of absorption), *Quwwat e Masika* (power of retention) and *Quwwat e Dafiya* (power of excretion).

In the meantime, some *Advia e Khareef* (hot spices) improve the digestion and absorption in the stomach partly by increasing the blood supply to the intrinsic vessels and thus resulting local vasodilatation which, in turn, enhance the bioavailability of the other drugs administered along with them. It has also been established that hot spices increase the transfer of therapeutic moieties or chemical substances across the gastrointestinal wall. Further, *Quwwat e Masika* (power of retention) and *Quwwat e Dafiya* (power of excretion) of other organs regulate the duration of activity of a particular drug without being affected by the rapid excretion through the kidneys or by sweating. Therefore, *Garam vo Khushk* mizaj drugs such as *Piper nigrum*, *Piper longum*, *Zingiber officinale*, *Carum carvi*, *Cuminum cyminum* and *Curcuma longa* are widely used.

#### **Bio enhancers in Ayurveda**

To achieve maximal effect of the drug Ayurveda formulations also generally incorporate *Yogvahi* (bioenhancers). It has been found that when these *Yogvahis* combined with an active drug they enhance the bioavailability of that drug at the site of action and potentiate its pharmacological effect<sup>6</sup>. To perform these actions, the hot potency (*Ushna veerya*) drugs such as *Piper nigrum*, *Piper longum*, and *Zingiber officinale* are used as *Yogvahi*. All these drugs increase the *Jathargni* (digestive fire or digestive power) located in the stomach. *Jathargni* is the *Agni* that is responsible for digestion, absorption and assimilation of drugs into more subtle substances which enters into the systemic circulation to exert the therapeutic effect<sup>9</sup>. In addition, these drugs are *Katu* (pungent), *Amila* (sour) or *Lavana* (salty) in taste and these tastes are

composed of *Agni*<sup>10,25</sup>. They also have actions like *Deepana* (digestive), *Sookshma* (entering deep and minute channels), *Teekshna* (piercing), *Grahi* (absorbent), *Rochaka* (appetizer) etc; which helps to promote digestion, improve blood circulation and enhances absorption<sup>11,12,13</sup>.

#### **Properties of drugs that act as bioenhancers**

- They are mostly *Garam vo Khushk* mizaj.
- They should be *Muqawwi e Hazim*.
- They are aromatic and impart flavour to the drug.
- It mostly possesses pungent, sour, salty or Bitter taste.
- It should be effective at very low concentrations.
- It should enhance the activity of the drug molecule<sup>1,6,8</sup>

#### **Possible mechanism of action of bioenhancers**

Different bio enhancers may have the same or different mechanism of action.

- Promoting the absorption of the drug from the gastrointestinal tract.
- Reduction in the hydrochloric acid secretion and increase in the gastrointestinal blood supply.
- Inhibiting or reducing the rate of bio transformation of the drugs in the liver or intestines.
- Inhibition of gastrointestinal transit, gastric emptying time and intestinal motility.
- Modifying the immune system in such a way that the overall requirement of the drug is reduced substantially<sup>1,5</sup>

#### **Benefits of bioenhancers**

Bio enhancers offer a comfortable, convenient, non-invasive way to administer drugs with the following advantages<sup>6,8</sup>

- Increased bioavailability.
- Reduced adverse drug reactions or side effects.
- Increased efficacy.
- Reduced drug dosage.

## Methodology

### Data collection

Pharmacopoeias (*Qarabadeens*) such as Unani Pharmacopoeia (UP), Handard Pharmacopoeia of Eastern Medicine (HPEM), National Formulary of Unani Medicine (NFUM), Impcops, Pharmacopoeia of Hospital of Integrated Medicine (HIM) were thoroughly scrutinized to find out the *Mufrad Dawa* (single drugs) commonly used in compound formulations (*Murakkab Dawa*) which do not possess any direct therapeutic indication to the purpose for which those formulations are generally used. Basic principles in Pharmacology (5<sup>th</sup> edition) by Mcgraw HILL Saunders Elsevier and Text book of Industrial Pharmacognosy (1<sup>st</sup> edition) by A N Kalia (2006) were also thoroughly studied to exploit modern aspects of Bio enhancing techniques. Google scholar, PubMed, WebMD, Medscape and MEDLINE databases were used to search journal articles from which current research outcomes relating to bio enhancers used in pharmacological formulations in Unani and Ayurveda were collected. The search terms (Bioenhancers, single drugs used to enhance bioavailability etc.) were used without narrowing or limiting search elements. Only the research studies in the English language were considered in the review.

### Study design

As the issues of poor therapeutic effect of the drug combination after the administration due to poor bioavailability have been established by a number of clinical studies, the purpose of incorporating certain *Mufrad Dawa* (single drugs) commonly in the Unani *Murakkab Dawa* were studied in Unani Pharmacopoeias. The concept of increasing bioavailability in Ayurveda formulations was extracted from authentic texts. Research articles were studied for a better understanding of ingredients or substances (chemical entities) which are used in *Murakkab Dawa* and to correlate the traditional wisdom or empirical knowledge of Unani System of Medicine with modern strategies. The knowledge of this study would open a new vista to understanding the combination of several ingredients into a single entity. Clinical trials or the

intervention therapy of selected drugs related to bio enhancers from journal articles were filtered. The journal articles from 2000-2018 were considered as eligible for this review.

### Database analysis

After collection the formulations in pharmacopoeias and reading materials were thoroughly scrutinized and filtered the *Mufrad Dawa* used to increase the bioavailability of compound drugs. Few of them are broadly described in this study. The final summary was formulated after a thorough reading of all reading materials.

## Discussion

In this study, five (5) Unani pharmacopoeias were scrutinized for effective *Murakkab Dawa* containing supportive ingredients in small quantities but they do not possess specific therapeutic effect as that of the main ingredient/s<sup>14,15,16</sup>. Approximately 180 Unani formulations that are supposed to hold a good efficacy in terms of Unani concept were randomly scrutinized from the Unani pharmacopoeias for their ingredients. Fifteen (15) ingredients were identified based on their role in the *Murakkab Dawa* as supportive ingredients that act as bio enhancers. Among these the following five ingredients were found to occur very commonly. Table 01 shows the presence of *Mufrad Dawa* (supportive ingredients) in *Murakkab Dawa*

**Table 01: Presence of *Mufrad Dawa* (supportive ingredients) in *Murakkab Dawa***

Supportive ingredients ( <i>Mufrad Dawa</i> )	Number of <i>Murakkab Dawa</i>	Percentage of presence out of 180
<i>Piper nigrum</i> ( <i>Fil fil e siyah</i> )	97	54
<i>Piper longum</i> ( <i>Fil fil e daraz</i> )	58	32
<i>Zingiber officinale</i> ( <i>Zanjabeel</i> )	94	53
Total number of formulations	180	



The above results showed that the supportive ingredients incorporated along with the main ingredient/s in almost all the *Murakkab Dawa* are used to enhance the bioavailability and thus the therapeutic efficacy is increased.

#### ***Fil fil e Siyah (Piper nigrum) and its bio-enhancing effects***

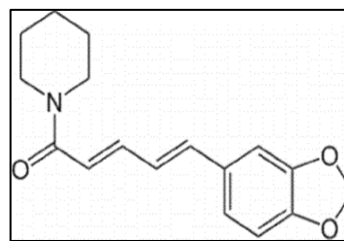
*Fil fil e Siyah* (black pepper) (Figure 01) is the most commonly used *Mufrad Dawa* in many compound formulations. Black pepper acts as *Muqawwi e Hazim* (digestive tonic), *Muqawwi e Kabidi* (liver tonic), *Muhallil e Riyah Ghaleez* (anti flatulence) and *Muqawwi e Meda* (stomachic) in these *Murakkab Dawa*<sup>11,21,22</sup>. Black pepper is also *Haar-Yabis* (hot and dry) drugs in third degree in *Mizaj* (Temperament)<sup>22,23</sup>.

According to Ayurveda texts, the Black pepper is pungent (*Katu*) in taste and pungent (*Katu*) in *Vipaka* (post digestive effect) which increases the *Pitta* in the stomach<sup>25</sup>. Further it is *Ushna veerya* (Hot) and it is a warming spice that has the qualities (*Guna*) like *Teekshna* (strong, piercing) and *Sookshma* (enters deep and minute body channels)<sup>9,11,18</sup>.

Recent research studies reveal that Piperine (Figure 02), the main alkaloid in the *Fil fil e Siyah* (black pepper) possesses bio enhancing or bio potentiation properties. Therefore, piperine is very useful for lowering the dose profile and shortening of treatment. It also acts as a nutritional bioenhancer which enhances the bioavailability and absorption of nutrients by acting on the gastrointestinal tract<sup>1,11,12</sup>.



**Fig. 01: *Fil fil e siyah***



**Fig. 02: Piperine**

#### ***Fil fil e Daraz (Piper longum) and its bio enhancing effects***

*Fil fil e Daraz* (Figure 03) is another important *Mufrad Dawa* incorporated in compound drug formulations. Long pepper acts as *Mushthahi* (appetizer), *Kasirriyah* (carminative), *Muqawwi e Meda* (stomachic), counter irritant in these *Murakkab Dawa*<sup>22,23</sup>. These actions favours the long pepper to be included as a bioenhancer. In addition, *Fil fil e Daraz* is temperamentally (*Mizaj*) considered as *Haar- Yabis* (hot and dry) drug in third degree (3°)<sup>22,23</sup>. The hot property of the drug enhances drug absorption and digestion.

According to Ayurveda, long pepper is a drug of pungent (*Katu*) taste with hot (*Ushna*) properties<sup>13,18,20</sup>. Other properties of long pepper are *Deepani* (improves digestion and strength) and *Pittaprakopini* (slightly increases pitta). Because of the hot property and pungent taste, *Pitta* and *Agni* are increased leading to improved digestion (*Deepana*). These factors contribute to bio potentiation<sup>13,24</sup>.

As in other pepper varieties, Piperine (Figure 02) is the active principle which is safe, and considered a natural and nutritive bio enhancer<sup>1,12</sup>.



**Fig. 03: *Fil fil e Daraz***

### Zanjabeel (*Zingiber officinale*) and its bio enhancing effects

Zanjabeel / Adrak (Figure 04) is also a very common drug incorporated in *Murakkab Dawa*. In those drug formulations, *Adrak* act as *Hazim* (digestive), *Kasirriyah* (carminative), *Muqawwi e Meda* (stomachic), *Mufatteh e Sudad e Jiger* (remove obstruction in liver), *Mushthahi* (appetizer)<sup>19,22,23</sup>. *Adrak* is *Garam 2°* and *Khushk 1°* (hot and dry) in *Mizaj* (Temperament) whereas, dried ginger (*Sont*) is *Garam 3°* and *Dry 2°* (hot 3° and dry 2°)<sup>22,23</sup>.

According to Ayurveda, Ginger is a *Katu rasa* (pungent taste) drug with an *Ushna veerya* (hot potency) which increases the *Agni* (Digestive power). It also possesses the properties of *Teekshna* (strong and piercing), *Rochaka* (appetizer), *Deepana* (digestive tonic) and balances *Kapha* and *Vata*. A special property seen in this herb is *Grahi* (absorbent) and bowel binding which is due to its hot property<sup>9,18,20</sup>.

In modern contexts, ginger is said to have a powerful effect on GIT mucous membrane. *Zingiberene* which is a terpenoid and phenolic compounds like *Gingerol* regulates the intestinal function to facilitate absorption<sup>11,18</sup>.



Fig. 04: Zanjabeel

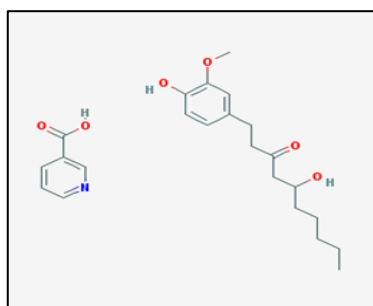


Fig. 05: C<sub>23</sub>H<sub>31</sub>NO<sub>6</sub>

### Discussion

#### Drug absorption barrier

After the administration, a drug must cross the epithelial barrier of the intestinal mucosa (Figure 06) for it to be transported from the lumen of the gut into the systemic circulation and exert its biological actions<sup>5</sup>. The structures of the intestinal epithelium serve as barriers to the transportation of drugs from the gastrointestinal tract to the systemic circulation. The membranes around epithelial cells are made of two layers of lipids containing proteins such as receptors and carrier molecules<sup>1,26</sup>.

Drugs cross the lipid membrane by passive diffusion or carrier-mediated transport. In the meantime, the hydrophilic nature of the aqueous stagnant layer of the epithelium is the potential barrier to the absorption of drugs with water-soluble molecules. As a result, small water-soluble molecules pass easily through the aqueous channels within the proteins whereas molecules larger than about 0.4 nm encounter difficulty in passing through these aqueous channels<sup>1</sup>. Therefore, several strategies have been developed to enhance the intestinal absorption of the poorly absorbable drugs.

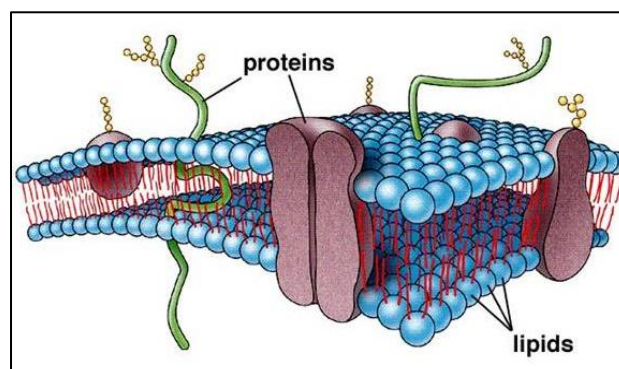


Fig. 06: Plasma membrane of gut epithelium

#### Modern methods to enhance the absorption of Drugs

##### Absorption enhancers

There are many substances that act as effective Absorption enhancers to improve the intestinal absorption, such as bile salts, surfactants, fatty acids and polymers. Bile, bile salts and fatty acids are surfactants which act as absorption enhancers by increasing the solubility of hydrophobic drugs in the

aqueous layer or by increasing the fluidity of the apical and basolateral membranes<sup>1,4,26</sup>.

#### **Dosage form and other pharmaceutical approaches**

Utilization of permeability-enhancing dosage forms is one of the most practical approaches to improve the intestinal absorption of poorly absorbed drugs. There are various dosage forms such as liposomes and emulsions that enhance the intestinal absorption of insoluble drugs to increase the absorption. Particle size reduction such as micronization, nanoparticulate carriers, complexation and liquid crystalline phases also maximize drug absorption<sup>1,4,26</sup>.

#### **P-glycoprotein inhibitors**

The application of P-glycoprotein (P-gp) inhibitors to improve the bioavailability of orally administered drug delivery has gained special interest. Several studies have shown that possible use of P-gp inhibitors reverse P-gp mediated efflux and thus, improve the efficacy of the drug transport across the epithelia<sup>1,4,26</sup>.

#### **Mechanism of action of Unani bio enhancers**

In the Unani system of medicine, the bioavailability of the drug formulations is increased by using herbal bio enhancers. Therefore, the actions of the *Mufrad Dawa* play an important role to accomplish this task. In this context, the action of *Mufrad Dawa* such as *Muqawwi e Hazim* (digestive tonic), *Muqawwi e Medha* (stomachic), *Kasirriyah* (carminative) and *Mushthahi* (appetizer) improve the digestion and absorption in the stomach. Whereas, the actions such as *Muqawwi e Kabidi* (liver tonic) and *Mufatteh e Sudad e Jiger* (deobstruent of liver) improve the proper liver digestion and thereby increase the bioavailability of the drugs.

*Fil fil e Siyah* possesses *Muqawwi e Hazim* (digestive tonic), *Muqawwi e Kabidi* (liver tonic), *Muhallil e Riyah Ghaleez* (anti flatulence) and *Muqawwi e Medha* (stomachic) and these actions are important in improving the bioavailability of the active moiety in the *Murakkab Dawa*. *Fil fil e Daraz* is another important *Mufrad Dawa* commonly found incorporated in compound drug formulations. These drugs also act as *Mushthahi* (appetizer), *Kasirriyah* (carminative), *Muqawwi e Medha* (stomachic),

counterirritant in these *Murakkab Dawa*. These properties increase the digestion, absorption and bioavailability of the drug. *Zanjabeel* is also found to be a very common drug incorporated in *Murakkab Dawa* which possesses *Hazim* (digestive), *Kasirriyah* (carminative), *Muqawwi e Medha* (stomachic). These actions of *Zanjabeel* also support digestion, absorption and bioavailability of the drug<sup>22,23</sup>.

In addition to these actions, *Fil fil e Siyah* and *Zanjabeel* possess *Muqawwi e Kabidi* (liver tonic) and *Mufatteh e Sudad e Jiger* (remove obstruction in liver) respectively. These actions improve the *Hazim e Jigeri* (liver digestion) and remove the obstructions in the liver resulting in enhanced bioavailability of the drug<sup>23</sup>.

Further, the supportive ingredients or *Mufrad Dawa* are *Garam vo Khushk* in *Mizaj* which increase the innate heat of the *Murakkab Dawa* and thus, facilitate digestion by increased blood supply to intestinal mucosa and cells.

*Fil fil e Siyah*, *Fil fil e Daraz* and *Zanjabeel* are *Haar-Yabis* (hot and dry) in *Mizaj* (temperament). Owing to this *Garam* (hot) property, the blood supply to the intestinal mucosa is increased which, in turn, increases the digestive power in the stomach. This also contributes to the increased bioavailability<sup>9,21</sup>.

In the Unani system of medicine, taste of the drugs also imparts a great importance in strengthening the digestive function. These drugs are especially categorized as *Adviya Khareefa* (pungent taste drugs), *Adviya Khushbudar* (aromatic drugs), *Adviya Murriya* (bitter drugs). Such drugs also possess the action of *Muqawwi e Hazim* (stomachic), *Kasirriyah* (carminative). In this context, the aromatic drugs *Fil fil e Siyah*, *Fil fil e Daraz* and *Zanjabeel* are good blend of volatile essential oils accredited with pungent taste capable of increasing the *Hararat e Medha* (innate heat in the stomach) leading to better absorption of drugs and its metabolism enhancing the bio availability.

In the Ayurvedic perspective, the drugs are classified based on the taste (*Rasa*) which contains six tastes. Each of the six tastes has an intimate



relationship with the *Doshas* and five main elements (*Pancha maha bhoota*). Out of the six tastes – pungent (*Katu*), sour (*Amla*), salty (*Lavana*) a crucial role in strengthening the stomach, enhancing the digestion by improving the *Agni*, increasing blood supply to the intestinal mucosal wall and thereby improves the bio availability of the drugs<sup>9,12,13,14,25</sup>.

Each taste is composed of two elements as per the basic elemental theory (pungent – fire and air, sour – earth and fire, salty – fire and water)<sup>24</sup>. Therefore, it is evident that salty, sour, pungent possess in-built *Agni* (fire) and thus these tastes increase the heat in the stomach, increase and strengthen *Pitta* responsible for digestion. Further they strengthen all the functions which need increase of innate heat such as metabolism, penetration and cleansing of channels. As a result, when the drugs with these tastes are incorporated in drug formulations, they increase the bio availability of other drugs<sup>9,25</sup>.

According to Ayurveda black pepper, long pepper and ginger are of pungent (*Katu*) in taste and hot (*Ushna*) in potency. Because of the hot property and pungent taste, *Pitta* and *Agni* are increased which in turn improves digestion (*Deepana*). These factors also contribute to bio potentiation. In addition, these drugs have the properties of *Teekshna* (piercing), *Sookshma* (entering deep and minute body channels), *Rochaka* (appetizer), *Deepana* (digestive tonic) which increase the digestion and absorption of the drugs. Further, long pepper is *Pitta prakopina* (slightly increased *Pitta*) which improves the *Deepani* (digestion and strength). Ginger has a special property called *Grahi* (absorbent) which increases the bowel absorption<sup>12,18,20,24</sup>.

Recent research studies reveal that Piperine, the main alkaloid in the *Fil fil e Siyah* and *Fil fil e Daraz* possess bio enhancing or bio potentiation properties. Therefore, Piperine is very useful for lowering the dose profile and shortening of treatment. It also acts as a nutritional bio enhancer which enhances bio availability and absorption of nutrients by acting on gastrointestinal tract. In a recent study, it has been evident that the absorption of curcumin is increased 2000 times when

incorporated with piperine<sup>27,28</sup>. Ginger contains Gingerol which regulates the intestinal function to facilitate absorption and thus, it improves the bioavailability of the drug<sup>1,2,5,9</sup>.

## Conclusion

This study opens up new scope of using herbal bioenhancers to improve bioavailability of poor absorbable and bio-available in *Murakkab Dawa* embedded in the concept of empirical designing of *Murakkab Dawa* in Unani system of medicine. Therefore, the commonly found supportive ingredients are considered as the key ingredients for digestion and absorption of the active therapeutic moieties which enhances the bioavailability of the drug. They may also enhance the therapeutic effect of the main drug, by presenting in small quantities in the *Murakkab Dawa*, to a great extent that can only be possible by giving large amounts of *Mufrad Dawa*. Therefore, it can be concluded that supportive ingredients collectively and synergistically act to overcome the poor absorption of the active therapeutic moieties and thereby increase the level of the active moieties in the blood.

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