



## Convoy Drugs in Traditional Persian Medicine: The Historical Concepts of Bioavailability and Targeting

Nastaran Ebadi<sup>1</sup>, Fatemeh Masoomi<sup>1</sup>, Maryam Yakhchali<sup>1</sup>, Seyede Nargess Sadati Lamardi<sup>1</sup>,  
Mohammad Reza Shams-Ardakani<sup>2</sup>, Omid Sadeghpour<sup>3</sup>, Azadeh Raiesdana<sup>1</sup>, Farid Ramezany<sup>1</sup>

<sup>1</sup> Department of Traditional Pharmacy, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran

<sup>2</sup> Department of Traditional Pharmacy, School of Traditional Medicine AND Department of Pharmacognosy, School of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

<sup>3</sup> Department of Herbal and traditional Medicine, Research Institute for Islamic and Complementary Medicine, Iran University of Medical Sciences, Tehran, Iran

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### Abstract

Similar to other traditional medicines, Traditional Persian Medicine (TPM) applies its special terms for description of drug functions. Among these functions, convoy (*Mobadregh*) medicines are unique, mainly due to the interaction of them with the pharmacokinetics of other herbal medicines. These interactions suggest the potential herb-herb and herb-synthetic drug interactions with convoy medicines that necessitate the study and precise definition of them. For this purpose, old Persian medical texts and pharmacopeias were searched and investigated for the name of convoys, their target organ(s), primary qualities, and other functions. Relationships among convoy and other functions based on notes on the texts and statistical analysis were considered. Based on the old resources, the convoys were defined as modifiers (of drug actions), which facilitate access of drugs and foods to whole body or organs. The concept of targeting in some convoys was also implied as well as other disciplines such as Traditional Chinese Medicine and Ayurveda. Descriptive analysis of the available data showed that most of the convoys contain warm and dry primary qualities. Anti-blockage and thin consistencies are main characteristics of this class of drugs. Statistical analysis also showed diuretic activity is another major characteristic of them. Other functions such as discutient, attenuant, and tonic are capable to assist conveying by thinning of humors and organs. Analysis of TPM literature shows the presence of a logic approach in the formulation of compound drugs. Owing to the potential influence of convoys on the pharmacokinetic profile of other herbs and synthetic drugs, it is necessary to conduct future studies to evaluate these interactions in TPM and modern medicine.

**Keywords:** Traditional Persian Medicine, Materia Medica, Herbal Drug Interactions, Drug Functions, Drug Targeting, Bioavailability

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Corresponding Author: Farid Ramezany  
Email: farid.ramezany@gmail.com

## 1. INTRODUCTION

Traditional Persian Medicine (TPM) is an invaluable experience resource of Persian pharmacists and physicians ancestors. Unfortunately, due to long recession period, lasted three centuries, some of these concepts are not only ambiguous in terms of contemporary medicine, but also for some traditional healers. To clarify the concepts, it is necessary to search, compare and decipher different literature of traditional medicine.

In TPM, drug properties were expressed as drug functions (*Afall*). Among the functions, conveying (*Badraghe*) is unique, mainly due to the relationship of this function with absorption and distribution of other drugs. In addition, there is a controversy among traditional healers about referring the concept of conveying to bioavailability, metabolism, and targeting or all of them.

In this overview, it was tried to describe convoys (*Mobadregheh*) by comprehensive search in TPM medical books, pharmacopeias, and formularies. Then, the relationship among conveying and other function were considered based on the literature. Afterward, the primary qualities and other drug functions related to convoys were analyzed by statistical methods to find out a possible relationship between the conveying and other drug functions. Finally, ambiguities respecting to synergistic and targeting effects were discussed.

## 2. METHODS

A number of old Persian medical texts and pharmacopeias were searched for keywords conveying (*Badraghe*) convoy(s) [*Mobadregheh(at)*] and to convoy (*Tabadrogh*) [1], [2], [3], [4], [5], [6], [7], [8], [9], [10]. Then, related texts (cf. Supplementary translated texts) were investigated for the name of convoys, their target organ(s) (Table 1), primary qualities (Figure 1) and other functions (Figure 2). Data analysis was carried out using SPSS (version 16, SPSS, Inc., Chicago, IL, USA). Relationships among the functions of convoys were analyzed using hierarchical clustering classification (Figure ). Finally, relationships among convoy

and other functions based on notes on the texts and frequency of possibly related characteristics were considered.

**Table 1.** The convoys used in TPM and their target organs

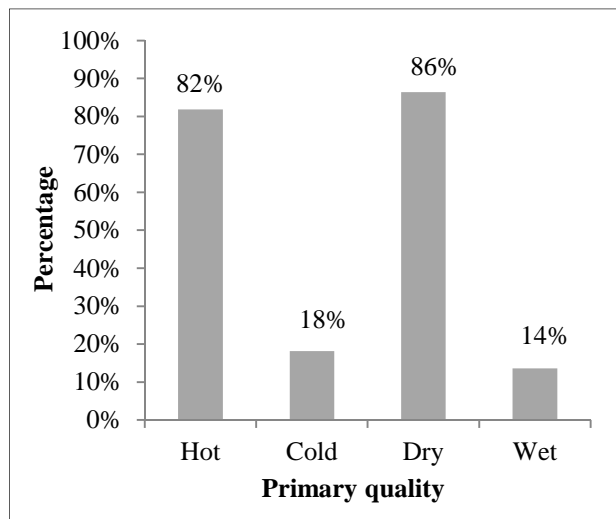
Common name (Proposed scientific name)*	Target organ(s)
Saffron ( <i>Crocus sativus</i> )	Heart vessels Brain vessels Other organs
Vinegar	Spleen Brain internal
Melon seeds ( <i>Cucumis melo</i> )	Liver Urinary tract
Zararih ( <i>Hycleus polymorphus</i> )	Kidney Bladder
Chicory seeds ( <i>Cichorium intybus</i> )	Liver
Celery seeds ( <i>Apium graveolense</i> )	Liver
Hazelwort rhizome ( <i>Asarum europaeum</i> )	Brain vessels
Tea leaf ( <i>Camellia sinensis</i> )	Stomach Body internal Body peripheral
Fennel seeds ( <i>Foeniculum vulgare</i> )	Body peripheral
White agaric ( <i>Polyporus officinalis</i> )	Body peripheral
Anise seeds ( <i>Pimpinella anisum</i> )	Non-specific (Acceleration)
Wild cinnamon bark ( <i>Cinnamomum iners</i> )	Non-specific (Acceleration)
Sassafras bark ( <i>Sassafras albidum</i> )	Non-specific (Acceleration)
Long pepper ( <i>Piper longum</i> )	Non specific
Dill seeds ( <i>Anethum graveolens</i> )	Non specific
Black pepper ( <i>Piper nigrum</i> )	Kidney stones
Horsemint leaf ( <i>Mentha longifolia</i> )	Kidney stones
Cinnamon bark ( <i>Cinnamomum zeylanicum</i> )	Kidney stones
Pine seeds ( <i>Pinus sylvestris</i> )	Not specified
Wine	Non-specific (Acceleration)
Camphor ( <i>Cinnamomum camphora</i> )	Heart
Water	Non-specific

\*In some cases, different scientific names were attributed to each convoy. Therefore, the most popular name was included as proposed scientific name. TPM: Traditional Persian Medicine

## 3. RESULTS

Table 1 represents the convoys and their target organs, which have been found by literature review. At a glance, the majority of convoys are specific for one or more organs. Acceleration of

drug effect is a mechanism for some of the non-specific convoys (anise seeds, wild cinnamon bark, sassafras, and wine). For other non-specific convoys, there is not any indication to the mechanism of conveying.

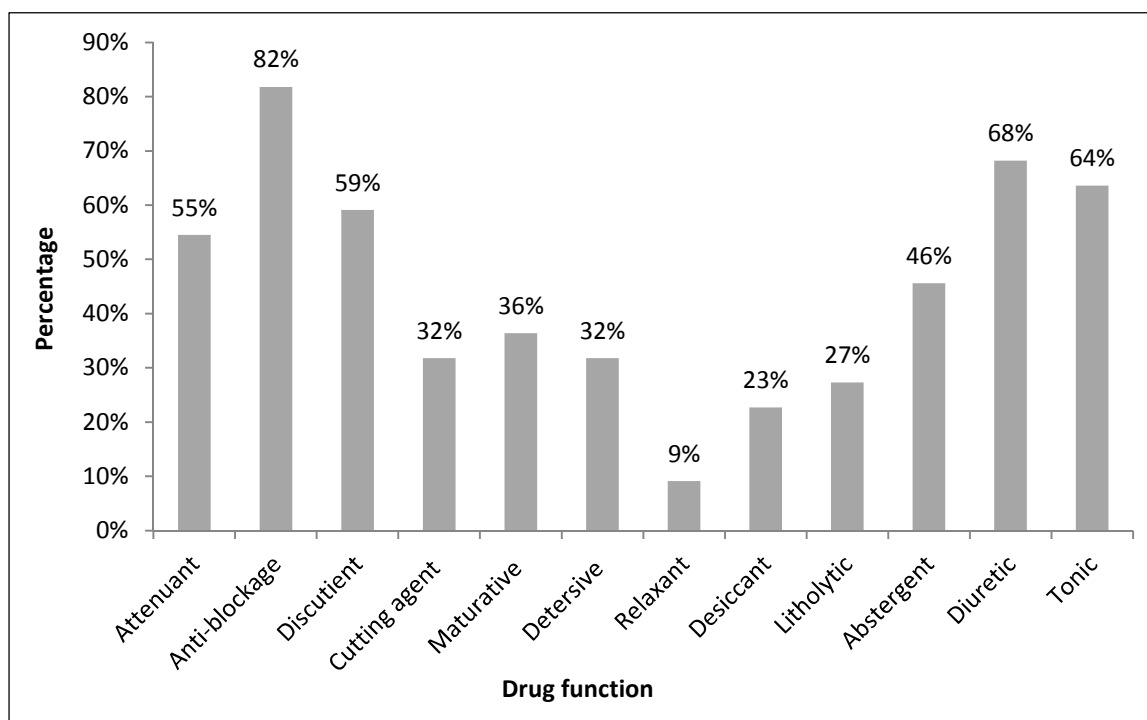


**Figure 1.** The frequency of primary qualities in convoys used in Traditional Persian Medicine

Figure 1 represents the frequency of primary qualities in convoys used in TPM [11], [12], [13]. Based on the result of the diagram, it is obvious that most of convoy

medicines are hot (82%) and dry (86%). In terms of drug functions, the most of convoys were mentioned in literature as anti-blockage (*Mofatteh*) [3] and thin (*Latif*) [2]. Consideration of drug functions of convoys in TPM showed that anti-blockage (82%), diuretic (*Moder*, 68%), tonic (*Moghavi*, 64%), discutient (*Mohalel*, 59%), attenuant (*Molatef*, 55%), and abstergent (*Monaghi*, 46%) are conspicuous (Figure 1).

Figure represents the scheme of classifying six conspicuous functions of convoys used in TPM. The lowest rescaled distance cluster combine (RDCC) was observed for discutient and diuretic functions that indicate a close relationship of this function to each other in convoys. The anti-blockage also clusters with these functions, though RDCC is  $> 15$ . This indicates that there is a moderate relationship between anti-blockage and discutient and diuretic cluster. By the same analogy, attenuant and abstergent functions belong to a same cluster, which implies a relationship between these functions. The highest RDCC was observed for a tonic function that indicates the lowest relationship among it and other studied functions.



**Figure 2.** The frequency of drug functions in convoys used in Traditional Persian Medicine. See supplementary section for more information about the functions

## 4. DISCUSSION

### *Literature*

In TPM, modification of lifestyle has priority over treatment. In the same manner, treatment with single, least side effects and low toxicity drugs was preferred to compound, high side effects, and toxic drugs, respectively. In this point of view, medical scholars tried to explain the conditions and reasons of compounding in medicaments. The drawbacks main drug(s) can be modified by two ways, processing (*Tadbir*) and use of another drug namely modifier (*Mosleh*).

A modifier was defined as a substance, which modifies the efficacy of foods and drugs. They were used for improving drug efficacy, reduction of side effects and masking unpleasant taste or odors. These goals could be achieved in several ways such as synergy, maintaining their effect (prevention from metabolism or stabilization of it in dosage form), sustaining drug release and conveying drug in whole body or specified organs [4], [14].

Based on these criteria, it is not surprising that convoys were classified as a type of modifiers in TPM [10]. In old authoritative literature, convoys were described as modifiers which homogenize, mix and/or guide the components (drug or food) to organs [1], [8]. In addition of these features, facilitation and speeding up characteristics were also emphasized [7], [9]. Therefore, it can be concluded the convoys are substances (or drugs) which, facilitate access of drugs and foods to whole body or organs.

Avicenna explained a number of mechanisms for increasing drug efficiency in organs by a combination of a drug with another drug [7]. It can be summarized as following routs:

1. Decrease in the digestion of main drug in an organ(s), which can be correlated to decrease or inhibition of its metabolism.
2. Facilitation and speeding up of main drug distribution to an organ(s).
3. In case of quickly absorbed drugs, decrease in absorption and distribution of main drug.

4. Targeting of the main drug by another to specified organ(s).

In TPM, the most of drugs contain hot and dry properties. This trend also maintains in convoys. Although there is not any direct explanation for this phenomenon in TPM resources, it could be concluded some of drug functions attributed to convoys (attenuant, anti-blockage, discutient, diuretic and cutting activity) originated from hot primary quality. No indication was found in investigated literature for deciphering dry primary quality.

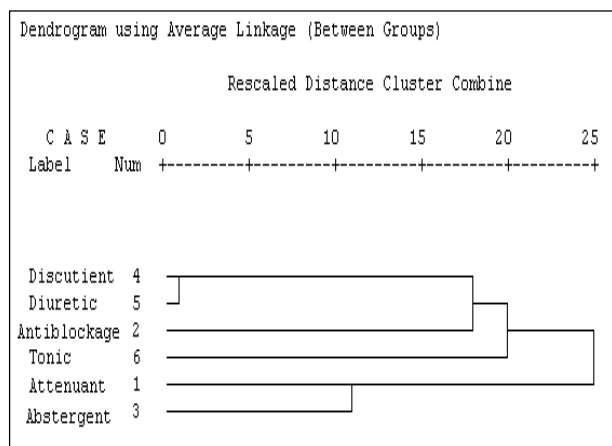
As indicated, the most of convoys hold anti-blockage function and thin characteristic. The flow of body fluids (humors) improved by reduction of blockage(s) in paths (veins, barriers, etc.). Therefore, nutrients and drugs can pass through them easier to reach the destination. The same conclusion could be drawn for thin convoys, which are able to diffuse better in humors and organ [15].

Among the other functions, attenuant is important in convoys, mainly due to the thinning activity of attenuant function leads to thin humors and consequently thin organs, which are more diffusible for drugs [15]. In TPM, some drug functions induced or enhanced by the contribution of the other functions. According to the old literature, attenuant function facilitates functions such as anti-blockage, maturative, diuretic and discutient [15]. Therefore, it is not surprising that maturative and discutient are present in convoys along with anti-blockage function. The same conclusion could be drawn from anti-blockage activity, which can contribute to cutting and discutient functions [4].

### **4.2 Functions Clustering**

At a glance, the relationship between functions seems complicated. Therefore, a hierarchical classification was applied for six more frequent functions to show the relationship of them in TPM convoys (Figure 3). Based on the classification results, the discutient and diuretic functions are more consistent. In the definition of these functions, the exclusion of unwanted material is a common feature. Therefore, it can be proposed what facilitates conveying also is

able to assist exclusion of materials. For instance, celery seeds and hazelwort convoy drugs to liver and brain vessels respectively while they also contain the diuretic function. This proposition also can explain why a considerable share of convoys related to the urinary system. Although anti-blockage activity clusters with discutient and diuretic functions, RDCC value is higher than a discutient and diuretic cluster. This result implied that anti-blockage activity is not related to exclusion of material from the body directly; but in case of some organs (kidneys etc.), it is able to assist exclusion. The attenuant-abstergent cluster remains unclear base on literature reviews though thinning of thick fluid and humors can facilitate movement of them and cleansing of the organs.



**Figure 3.** Hierarchical clustering of the six most frequent functions of convoys used in Traditional Persian Medicine

An interesting aspect of convoys function is a tonic function. The significant frequency of this function (64%) and clustering pattern of it suggests that tonic function is relatively independent of other functions. The possible explanation for this finding might be balancing of organ consistency, what returns to its definition [4]. This balance may improve drug affinity to target organ(s). Although there is an indication about the affinity of convoy and organ is important in conveying function [9], this mechanism must be confirmed with more evidences from recent and old literature.

### 4.3 Convoy Dosage

Based on TPM resources, the amount of convoy used in formulation is often lower than therapeutic doses. It is interesting to note that many convoys can hold both synergetic and conveying functions at the same time in a particular formulation. In these cases, formulator is able to use only conveying effect, by using lower amount, less than therapeutic dose, or apply both effects by using conveying effect in therapeutic level [5], [7].

### 4.4 Targeting in TPM Convoys

In TPM texts, convoy medicines can accompany main drugs to the specific organ(s), internal or peripheral compartment(s), and the whole of the body (Table 1). The affinity of some convoys for specific organs suggests targeting effect of them to those organs. On the other hand, the majority of specific convoys has an effect(s) on target organ(s), suggesting synergistic effect with the main drug. This phenomenon can be explained by two reasons. First, as stated, the dosage for conveying is less than effective therapeutic dose of the convoy on the target organ. Second, all specific convoys also affect organs other than target organ(s), but they have not conveying properties on them. In theory, it is quite reasonable that there are some pharmacology active constituents in herb, which accompanied by conveying constituent(s) to target organ. Unfortunately, the mechanisms of targeting were not asserted in TPM texts. The increase in the rate of reaching main drug to target organ and increasing the permeability of organ to main drug are probable mechanisms for this effect. Although there are some research articles in targeting effect of traditional Chinese medicine for targeting effect [16], [17], [18], future studies are required to prove it in TPM.

As shown in Table 1, there are some non-specific convoys, which accompany drug to the whole of the body. Decrease in digestion (metabolism), acceleration of absorption (probably intestinal absorption) are

mechanisms that proposed by Persian scholars for conveying these drugs. Similar to specified convoys, future studies are necessary to evaluate it in TPM and potential interaction(s) of them with other herbs or synthetic drugs.

## 5. CONCLUSION

Analysis of TPM literature shows the presence of a logic approach in the formulation of compound drugs. The convoys are a group of modifiers, which facilitate access of drugs and foods to whole body or organs. Factors such as rate of absorption and distribution, metabolism (digestion), targeting and its distance (internal and peripheral compartments) were considered important in convoy function. Literature reviews demonstrated the majority of convoys contain anti-blockage function and thin characteristic. Statistical analysis showed that the most of convoys have hot and dry primary qualities. In addition to anti-blockage function, diuretic, tonic, discutient, attenuant and abstergent are significant. The basic mechanisms for convoys are removing of blockages and

improving diffusion (thin characteristics). Other functions except tonic were attributed to these basic factors based on literature and cluster analysis. For tonic function, the effect on destination organ(s), probably with balancing of organ consistency, proposed to explain this observation.

In general, amount of convoy drug in the formulation is less than therapeutic dose. However, it is quite possible to use both conveying and synergistic functions of a drug in the formulation. The convoys can be specific for organ(s), accelerate absorption and non-specific. Although there are some explanations for this phenomenon, more studies are required to validate targeting activity in TPM convoys. Owing to potential influence of convoys on pharmacokinetic profile of other herbs and synthetic drugs, it is necessary to conduct future studies to evaluate these interactions in TPM and modern medicine.

## 6. CONFLICT OF INTERESTS

Authors have no conflict of interests.

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## SUPPLEMENTARY TRANSLATED TEXTS

“A physician should not use drugs if he can cure with foods and should not apply compound drugs if he is able to use single (unblended) drugs [9].”

“It is possible that the effect of a simple/single drug is in a right way, but we want it goes and treats far organs. We worry that the drug is disabled while pass through long paths by first and second digestion. Therefore, we convoy a drug as a guard which protect it at first and second digestion stages and bring it to desired destination safely like usage of opium inclusion in antidote [7].”

“There is a simple drug that is good and trustable. However, the risk of delaying to reach to the destination exists. We accompany another drug with it to prevent from delaying and deliver it to desired position in right time. In the same manner, when saffron mixed with camphor tablet, it guides camphor to target organ. As soon as camphor tablet reaches the heart; saffron separates from it and finished its function. On the other hand, camphor tablet itself separates cold-inducing and extinguishing drugs without saffron assistance. This division and categories could be found in many natural and synthetic (artificial) drugs. When compound drug reaches to the desired position, the reception power will be absorbed, and its repulsion power will be repulsed. Each of them accomplishes their duties. The discutient arrives directly to painful limb and dissipates pain-originating substance. Repulsion receptor blocks the pain originating substance path to inhibit assistance of external matter to the internal, accumulated one in the painful limb [7].”

“Sometimes it is required to use a drug which must pass slowly through internal body and delay to accomplish the worthwhile task in its passage. However, it is too fast. We have to accompany a drug to delay it in its ways and act properly. That is the case in the fast anti-blockage drugs, which pass through the liver quickly and immediately. We may want that the main drug stays in liver for a while and not pass quickly. Therefore, we mix a

drug (modifier) with anti-blockage main drug, which drives it to the opposite direction of liver. The main drug goes, and the modifier drives it not to go. The main drug has enough time to take function in natural, desired manner in the liver. For instance, we convoy radish seeds with liver anti-blockage drug. The seeds pull main drug toward the stomach, and it resists. In this combating the drug operates in a right way [7].”

“A simple drug might be bilateral. The main drug has effects in both aspects, but sometimes we want one of these affections. Therefore, we add a drug with it to escort it in just only one passage and inhibit it from other ways. For example, we mix diuretics and anti-blockages with zararih in this case; zararih application is to inhibit entrance of main drug to veins and diverts it to kidney and bladder [7].”

“The explanations of drug’s combination for organs are: There is an organ which is farther to stomach such as kidney, bladder and lung and the drug’s power reaches to them lately. Therefore, for drugs used for these organs, it is necessary to add a drug (another component) to guide them quickly and another drug to preserve the power of main drug by preventing digestion (metabolism) of main drug in other organ. The components that convoy to the site of effects are celery seeds, wild cinnamon barks and anise seeds. Physicians called these drugs *Mobadregh* in Arabic that means convoy. Those preserve, the power of drug by preventing digestion by another organ are opium, henbane seeds and mandrake root shells. If there is an organ which (main) drug should waits and stays on it for a while until complete function, such as liver and anti-blockage drugs, a small amount of another drug, such as radish seeds, was added to pull drug to the opposite direction (toward stomach). The main anti-blockage drug tends to open liver blockages and exit the liver quickly, but another drug (radish seeds) drive it to the opposite direction and make it wondered. Therefore, the anti-blockage drug stays on liver until exert its whole functions [9].”

“... Third, the (main) drug is weak in



potency and efficacy which loses them and becomes weak before reaching to the desired organ. Alternatively, owing to far distance of affected organ, its power (efficacy) becomes weak and lost or due to lack of organ affinity, it diffuses and scatters on its path and the power of drug cannot reach to the organ. Alternatively, the main holds organ affinity (in traditional medicine believed that there is special affinity between medicine which allocated to cure disease and damaged organ), but is not able to achieve by itself. Therefore, it requires combining with a fast penetration, organ affinitive drug, which strengthens and inhibits diffusion to convoy power and faculty of (main) drug to target organ, such as saffron in camphor tablets and heart drugs. Camphor also used in heart drugs to convoy the cooling effect of itself and other drugs to heart without much reduction, due to saffron and camphor affinity to the heart.

The property of saffron is to convey of drug effects to the heart by its heating power, its own property and reaction of (main) drug with homeostatic system, the effects of saffron will be canceled and the effect of drug remained. For this reason, the weight of saffron is less than camphor in camphor tablets. Like (saffron), camphor weight is less than other drugs in heart (compound) drugs to not overcome (other drug properties), become assistant and convoy of them.

Addition of vinegar in spleen drugs and saffron and asarum with scammony and agaric to transfer the power of them to brain and its veins to do their activities properly are included in this category. Zararih (probably *Hycleus polymorphus*) also could be added to diuretics useful for kidney and bladder, as a result of affinity to them, for conveying the power of the (diuretic) medicines to the organs quickly and perfectly [5].”

“Modifier: Something that modifies the state of eating and drinking materials including elimination of side effects, synergy, stabilization, lighten overpowering or conveying to organs [14].”

“Modifier: Something that modifies the state of eating and drinking materials, like

tragacanth, which is modifier of horse mint, synergism like mixing torpicum (torbod) with ginger, stabilization like combination of medicines with honey, lighten overpowering such integration of tragacanth with scammony or conveying the power of medicine like incorporation of zararih with diuretics [6].”

“Convoy (*Mobadreg*): Messenger; conveying matter; something that holds the properties of purifying component(s), and also mixing and conveying them to organs, like the function of wine on foods [1].”

“Convoy (*Mobadreg*): Something that is capable to crash another thing which mixes with it and permeate into (body) organs like water which do the same with foods and deliver the vital power to them [8].”

“... but assistants are something that share in main activity which was discussed in second section of tonics, desiccants and abstergents. Whatever is considered as a convoy and accompany medicinal effect into deep parts of the body is anti-blockage such as fennel, celery seeds, saffron etc. [3].”

“... it should be noted that we mix vinegar with rose oil extract in brain and meninges inflammation for conveying and accompanying the oil to brain ventricles; not for discutient benefits but for its thin character [2].”

“... and this recipe has nine components and its temperament is hot and dry at end of second degree. The main drug is aloes and cinnamon is incorporated for its tenuous character to convoy it [4].”

“Drug ingredients, which permeate litholytic main drug to the location of kidney stone faster, include pepper, horse mint, and cinnamon. In addition to conveying ability, these drugs are effective in moving stone [7].”

“Vinegar is desiccant, rapidly penetrative, attenuant, cutting agent of thick humor and convoy of medicines functions and powers to spleen. This affinity (between vinegar and spleen) originated sour taste of melancholy in spleen. Because spleen is a porous organ, which melancholy humor is refined on it, its beef is porous to absorb thick melancholy humor. It has many vessels, which causes more warmness; this warmness counteracts to coldness of

melancholy and digests it. This is the reason of vinegar affinity to spleen and capability of it for conveying of spleen drugs [9].”

“Anti-blockage medicines mobilize humoral materials, which stay in tracts, pores and inside of organs and move materials outward to open them. Attenuant medicines are drugs, which make other substances thinner. Actually, attenuant medicines lower consistency of humors. This function is not the outcome of coldness because coldness causes compression and contraction of substances and is not for dryness and wetness (passive primary qualities, not active). Therefore, it is only the outcome of hotness. The thinning function of attenuants is helpful in three ways:

- Maturation: Maturation of thick materials is achieved by thinning humors. Additionally, if these substances are viscous, drugs such as vinegar and spicy and sharp substances are useful, because they are both attenuant and cutting agents.

- Blockages opening: Thinning of blocking materials facilitates diffusion of them from their locations. The attenuants, which contain deterrent and/or abstergent functions, are better anti-blockages.

- Discutient function on thinned substances is easier. Therefore, when discutient activity is required, attenuants are used [10], [15].”

- Terminology of some words in TPM:

- Thin material (*Latif*): Material, that is capable to divide to very small particles after entering into and penetrates quickly in all compartments of the body.

- Anti-blockage (*Mofateh*): Medicines that mobilize humoral materials stayed in tracts, pores and inside of organs and move

materials outward to open them.

- Discutient (*Mohaleh*): Medicines that cut humors from their position separates their components and excrete them in vapor form.

- Attenuant (*Molatef*): Medicines that make thick humors thin by mild hotness.

- Cutting agent (*Moghate*): A thin medicine that penetrates between attachment surfaces of thick humor, separates its components, and excretes it in the shape of smaller segments.

- Detersive (*Jail*): A medicine that mobilizes thick and/or viscous wet materials and excretes them from organ(s) and pores surfaces.

- Maturative (*Monzej*): A medicine that moderates humor consistency.

- Tonic (*Moghavi*): A medicine that moderates organ consistency and temperament.

- Diuretic (*Moder*): A medicine that drives out and excludes water content of foods and body fluids wastes by urination, menstruation, sweating and lactation. This is done by hotness and discutient functions.

- Relaxant (*Morkhi*): A medicine that softens and widens the inflexible pores of the organs to facilitate discharge of confined waste materials from them. This is done by hotness and wetness.

- Litholytic (*Mofatet*): A medicine that crashes solidified and adhesive humors and make them fine and soft. This is done by sharpness and penetrative functions.

- Abstergent (*Monaghi*): A medicine that cleanse organs completely from wastes.

- Desiccant (*Mojafef*): A medicine that make organs dry. This is done by attenuant and discutient functions on wet materials.