Title: Galen's Introduction On Pharmacology As It Appears In The 3rd Book Of "De Temperamentis" *

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Introduction

Galen of Pergamus (129 A.D. - 201 A.D.) is one of the most important physiognomies of medicine during the Greek-Roman period. Apart from being a talented doctor, Galen was also a leading doctor in anatomy, physiology, pathological anatomy. He is the doctor who, for the first time, set the basis for a significant system of therapeutics that influenced medicine until the 15th century. Moreover, the famous motto "Galen said¹" of the 16th century marked any medical doubt during the 16th century. Consequently for more than 14 centuries Galen's authenticity was considered to be similar only to Hippocrates himself.

Galen was also a scholar who has written too many works and undoubtedly the most productive medical author in antiquity. According to Professor Jean Irigoin his entire work represents the 1/8 of what has been saved from the ancient Greek literary production, in the period from the days of Homer till the end of the second century $A.D^2$.

Apart from being such a talented doctor, Galen contributed with a large number of medical books in the development of pharmacology. The researcher who is interested in Galen's pharmacological work confronts his admonition to start the study from the third book of the work "on mixtures" "Περί Κράσεων". This work is a brief treatise on basic, fundamental and introductory pharmacological issues. There Galen, using simple ways, explains a series of important introductory ideas in pharmacology, totally necessary in the science. Afterwards the researcher will be able to handle and fully understand the most important of his main pharmacological studies "On Properties of simple drugs".

Galen's work "On Mixtures" refers to the main core of his medical thought. It's the cornerstone of the theoretical part of Galen's "medical construction". Never before him any doctor, not even Hippocrates, had achieved to systemize existing medical knowledge so as to create a complete theoretical medical system which would include both the medical practice and the cure of the patient. Galen himself emphasizes on the great importance of the work "on mixtures" ("Περί Κράσεων"). This is proved by the great number of references to this treatise in many of his other works 4 .

The word "κράσις" derives from the ancient Greek verb "κεράννυμι / κεραννύω" that means mix, combine, and compose. The term "κράσις", "mixture", as it is interpreted and approached by Galen, refers to "the person's general physical condition". According to Galen this mixing is identical with the combination of the hot, cold, wet and dry substances, as it is reported in the Hippocratic Corpus.

It is true that the theoretical background of the work "on mixtures" is the Hippocratic treatise "On the nature of man". Hippocrates was Galen's model. Galen

¹ Tsouras S., Lessons in History of Medicine, Vol. A, pg 169

² Irigoin J., *Tradition et Critique des Texts Grecs*, pg 255.

³ Gal. Ars Medica (1, 407-408 Kühn): περὶ μὲν οὖν τῶν καθ' Ἡπποκράτην στοιχείων εν βιβλίον ἐστίν. ἑξῆς δ' αὐτῷ τρία περὶ κράσεων. ὧντὰ μὲν δύο περὶ τῶν ἐν τοῖς ζώοις ἐστὶ κράσεων, τὸ τρίτον δὲ ὑπὲρ τῶν ἐν τοῖς φαρμάκοις. διὸ καὶ τὴν περὶ τῆς τῶν ἁπλῶν φαρμάκων δυνάμεως πραγματείαν οὐχ οἶόν τε κατανοῆσαι καλῶς ἄνευτοῦ τὸ τρίτον ἀκριβῶς ἀναγνῶναι περὶ κράσεων.

⁴ Moran Anne-France Morand and André-Louis Rey, *Elements, Humours and Qualities in Galen's Thought: One System or Many?*

himself admits that in his works his objective was to improve and complete what was left incomplete by Hippocrates⁵.

⁵ Tsekourakis D., *Galen: On Matters of Health*, pg 31

The humoral theory

Galen is faithful to the Hippocratic humoral theory which he extended by presenting his own theories in the three books of the work "on mixtures". In his effort to connect this study to Hippocrates himself, that he seems forget to mention the fact that the author was Polivious, Hippocrates' son in law. This is testified by Aristotle and Menon⁶. The four humor theory that is described in the work "on the nature of man" is of fundamental importance and absolutely necessary for the construction of Galen's theory as it appears in the treatise "on mixtures".

According to the humoral theory⁷, the ingredients of the human body are four

According to the humoral theory, the ingredients of the human body are four humors: the blood, the phlegm, and the yellow bile and black bile. These four humors result from the synthesis of the four basic elements which are: the earth, the air, the fire and the water. Each one of these elements gives to the human body a certain quality; earth gives dry, air-cold, fire-hot and water-wet. These four elements and their equivalent qualities compose the four humors that consist the human body. The formation described above results from mixing two of these elements: hot and wet becomes blood, hot and dry becomes yellow bile, cold and wet becomes phlegm and finally cold and dry becomes black bile. When humors are mixed, in certain quantities in the body, a balance is achieved. Health lies in this balance. In other words, the symmetric mixing ($\epsilon \nu \kappa \rho \alpha \sigma(\alpha)$) of the four humors is responsible for the good health. On the other hand, a disorder in the mixing ($\delta \nu \sigma \kappa \rho \alpha \sigma(\alpha)$), when one of the humors prevails or separates from the rest and gets independent, results to illness.

Humoral Pathology is also supported by Galen in his work "The elements according to Hippocrates" where the elements that compose the body are divided in opposite pairs: hot-cold and dry-wet. Each one of them may dominate to its opposite one, or the elements in one or in both pairs may be in balance.

⁶ Tsekourakis D., *Hippocrates: On nature of man*, pg. 26 – 27.

⁷ Hipp, On nature of man (cpt. 4, line 1-7 Tsekourakis D.): Τό δὲ σῶμα τοῦ ἀνθρώπου ἔχει ἐν έωυτῷ αἷμα καὶ φλέγμα καὶ χολὴν ξανθὴν καὶ μέλαναν, καὶ ταῦτ΄ ἐστίν αὐτῷ ἡ φύσις τοῦ σώματος, καὶ διὰ ταῦτα ἀλγεῖ καὶ ὑγιαίνει. Ύγιαίνει μὲν οὖν μάλιστα, ὅταν μετρίως ἔχη ταῦτα τῆς πρὸς ἄλληλα κρὴσιος καὶ δυνάμιος καί τοῦ πλήθεος, καὶ μάλιστα μεμιγμένα ἢ ἀλγεῖ δὲ ὅταν τοὐτων τι ἔλασον ἤ πλέον ἢ ἢ χωρισθῆ ἐν τῷ σώματι καὶ μὴ κεκρημένον ἢ τοῖσι σύμπασιν.

"On mixtures"

Here is a brief approach to the main points of this very important treatise. First of all it is composed of three books. The first two books deal with the different types of mixtures and their characteristics. The last third book, although it is a part of the trilogy, is independent in a way as it is an introduction in pharmacological issues⁸.

In the first book Galen defines the mixtures. Through a very detailed logical procedure of reasoning he rejects all opposing theories. He concludes that there are nine kinds of mixtures⁹.

First of all nine is the perfect mixture, which is perfectly balanced and no surplus exists amongst humors. As perfect mixture Galen couldn't name other than the perfect and healthy organism¹⁰; the type of human that has such a mixture is the measure for comparison and classification of all the remaining organisms. As mentioned above, in this mixture the pairs of opposites, hot-cold and dry-wet, are perfectly balanced. The same reasoning applies to the parts of the human body. Each part of the body has its own mixture by nature. For example the part which has the perfect mixture is the skin, and precisely the one that covers the palm of the hand¹¹.

The next four mixtures are called simple. They result when there is ill balance in a simple sense. One of the two opposite pairs is in balance but the other is not, due to prevalence of one of the two components. These four simple mixtures, in which ill-balance is seen, are: hot, dry, cold and wet. For instance, in the hot mixture the pair wet-dry is totally balanced, but between hot and cold the scales turn in favor of hot which is in surplus.

The last four mixtures are called "combined" as they result when there is ill balance in a composite sense and they are: a) hot and dry, b) hot and wet, c) cold and dry and d) cold and wet. These combined mixtures result from the surplus of each opposite pair. For instance, when the complex is hot and wet there is the domain of hot upon cold on the first pair and the domain of wet upon dry on the second at the same time.

Throughout **the second book** he deals with the properties and characteristics of anything that in nature is characterized by hot, cold, wet and dry. The characteristics of each kind of mixture concern not only the human as a whole being, but also the mixture of each organ separately. This point is extremely crucial for the selection of the right treatment of the patient that has ill balanced humors. This ill balance (dyscrasia) does not obligatory concern the whole body but may concern a very certain organ. Consequently the pharmacological treatment must selectively

 $^{^8}$ Gal. De ord. libr. sour. ad Eug. (19. 55-56, Kühn): ἐν μὲν οὖν τοῖς πρώτοις <περὶ κράσεων αἱ ἐν τοῖς> ζώοις <κράσεις> λέγονται μετὰ τῶν ἰδίων ἑκάστης γνωρισμάτων, ἐν δὲ τῷ <τρίτῳ> περὶ τῆς τῶν φαρμάκων κράσεως ὁ λόγος ἐστίν

⁹ Gal. De Temp. (1. 559, Kühn): ἐννέα τὰς πάσας εἶναι τῶν κράσεων διαφοράς, εὔκρατον μὲν μίαν, οὐκ εὐκράτους δὲ τὰς ὀκτώ, τέτταρας μὲν ἁπλᾶς, ὑγρὰν καὶ ξηρὰν καὶ ψυχρὰν καὶ θερμὴν, ἄλλας δὲ τέτταρας συνθέτους, ὑγρὰν ἄμα καὶ θερμὴν καὶ ξηρὰν ἄμα καὶ θερμήν καὶ ψυχρὰν ἄμα καὶ ὑγρὰν καὶ ψυχρὰν ἄμα καὶ ξηρὰν.

 $^{^{10}}$ Gal. De Temp. (1. 564-565, Kühn): ἀλλὰ καὶ τῶν ἄλλων ἁπάντων σωμάτων εὐκρατότατος ἐστιν ὁ ἄνθρωπος, ἄμα δ΄ ὡς τῶν ἐν αὐτῷ μορίων τὸ τῆς χειρὸς δἑρμα τὸ ἔσωθεν ἀπάσας ἐκπέφευγεν ἀκριβῶς τὰς ὑπερβολάς.

¹¹ Gal. De Temp. (1. 563, Kühn): Τοιοῦτον δ' ἐστί καὶ τὸ τῶν ἀνθρώπων δέρμα, μέσον ἀκριβῶς ἀπάντων τῶν ἐσχάτων, θερμοῦ καὶ ψυχροῦ καὶ σκληροῦ καὶ μαλακοῦ, καὶ τούτου μάλιστα τὸ κατὰ τὴν χείρα.

reverse the dyscrasia of that very certain organ and thus restore the health of that organ.

In order to fully understand this theory, a classic example is to be used as by Galen himself. We suppose, says Galen, that someone's perfect mixture of the belly has changed becoming hotter. Then he uses wild lettuce, which by nature is a cold medicine to restore the balance of the mixture and cure the patient. As the patient consumes a lettuce the latter freezes his belly. This reduces the temperature of that certain organ to its previous balance.

Investigating and understanding Galen's **third book** of "on mixtures" is of our special interest in this report. According to Galen, of the three books of the work "on mixtures", the two of these concern mixtures in animals, while the third concerns mixtures in medicines. In a way, it is an independent book. Thus, the work "On properties of simple drugs" cannot be properly understood without a careful reading of the third book of Mixtures.

"ON MIXTURES" Book III

Galen's third book is unique in its construction from the first glance. Using his theoretical innovations he introduces in the field of pharmacology the qualities (hot, wet, cold, and dry) of the four primary elements (water, air, fire and earth). From the mixture of the four primary elements microcosm and macrocosm are formed. This was a very important stopover in pharmacology. Galen connected the humoral pathology with the concept of the drug, developing a theoretical model which could describe the functional mechanism of the drugs in the human body.

Galen was very careful during the writing of this third book. In comparison to his previous works his writing is more accurate and dense, while his enmity to other doctors and colleagues is subsided. He is still fighting them but he seems not to have the urge to defend his work so passionately. He rarely mentions his opponents and if so he is really short in length and without exaggerations. His objective is mainly pedagogical. He introduces the reader into pharmacology. If the researcher can not follow his way of thinking or his methodology, it will be impossible to understand the other pharmacological works of Galen, and especially his new approach in the cure of the patient with drugs, at least at a theoretical level. The author knows very well that his effort to give flesh and blood in a theoretic pharmacological model has never been attempted before in medicine. That is why Galen is one of the greater doctors of ancient times. He could propose innovations, could organize them in a theory and finally organize a model using his scientific prestige.

FOOD AND DRUGS

Galen in order to develop his ideas about the meaning of drugs and their functional mechanism, initially, he describes in the simplest way the digestive mechanism. He avoids the exaggerative reports, for example the "platonic three spirits", and focuses to the main subject. He mentions the four fundamental forces ¹² that act to every human organism, in the way he has already described them in the book "on natural faculties". These four faculties of the body as a whole are:

- a) That which attracts useful substances,
- b) That which retains these,
- c) That which transforms substances, and
- d) That which expels alien substances.

According to Galen, in the human body exist four different, but totally balanced faculties. The sum of these faculties can be described by the digestion process. In every human body substances come into the body through swallowing. Initially due to the attraction faculty they are captured and then they are divided to useful and useless. The faculty that retains these acts then and engages the useful substances. In the next step the faculty acts that transforms then and assimilates them to the body and nourish it. Finally, the fourth faculty acts to expel the alien substances. That one can called "faculty of excretion" and discharges through three

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¹² Gal. De Temp. (1. 654, Kühn): ἀλλὰ μᾶλλον ἐκεῖνο διελέσθαι δικαιότερον, οὖ τὴν μὲν ἀπόδειξιν ἐν τοῖς Περὶ φυσικῶν δυνάμεων ἐροῦμεν, ἐξ ὑποθέσεως δ' ἂν ἕνεκα τῶν παρόντων καὶ νῦν αὐτῷ χρησαίμεθα, τέτταρας μὲν εἶναι παντὸς σώματος δυνάμεις, ἑλκτικὴν μὲν τῶν οἰκείων μίαν, ἑτέραν δὲ τὴν τούτων αὐτῶν καθεκτικὴν καὶ τρίτην <τὴν> ἀλλοιωτικὴν καὶ τετάρτην ἐπ' αὐταῖς τὴν τῶν ἀλλοτρίων ἀποκριτικήν, εἶναί τε ταύτας τὰς δυνάμεις ὅλης τῆς οὐσίας ἑκάστου τῶν σωμάτων, ἣν ἐκ θερμοῦ καὶ ψυχροῦ καὶ ξηροῦ καὶ ὑγροῦ κεκρᾶσθαί φαμεν.

main physical procedures, which Galen had already described. This preliminary presentation of the four faculties that dominate to the human body is very valuable for the definition of the functioning mechanism of the drugs.

Understanding what is a drug and the way that drugs act needs a thorough presentation of their mechanism of function. If this mechanism is not clearly understood we cannot present the drug or define the term.

As mentioned above, every substance that enters the human body will go through a certain process in the digestive organs, the stomach, the liver and the veins through which the body is nourished ¹³. This procedure results in blood formation which will be transported through the veins to the whole body ¹⁴ and flesh will be formed. The flesh is necessary to achieve homeostasis of the body. In parallel, as a side effect the internal natural heat rises. Every body, according to Galen, has a standard natural internal heat. Each time that a new substance is consumed and assimilated by the organism a new quantity of heat is added to the existing internal natural one ¹⁵ and so the heat increases. In this case, the sense of time should be taken into account. The introduction of the parameter of time which in this first approach is used in the process of digestion will be presented later in the mechanism of drug action during time.

In the case we study, though food gives additional heat to the body, as Galen remarks, this is not happening at once but after a period of time ¹⁶. During this crucial time period the natural temperature of the body decreases significantly. In this time a series of physiological functions take place, which use up all the energy in order to meet the organism's demands. We could call this procedure "equation battle", as Galen notes "when two substances exist in the same area (that is the stomach) they fight each other. In the end, both of them will have an effect and will be affected ¹⁷". In other words, the humors are in a continuous dynamic balance. This balance may change under certain circumstances. In such a case, one of the four humors prevails and as a result a serious illness manifests. However, when the "battles" in the human body disease the substance is assimilated and the balance among the four humors is restored. On one hand the substance is transformed to blood, and at the end of its assimilation the internal heat rises.

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 $^{^{13}}$ Gal. De Temp. (1. 662, Kühn): ὅθεν καὶ τρέφει καὶ ῥώννυσι τάχιστα. πάντως μὲν οὖν καὶ τοῦτον ὁμιλῆσαι χρὴ τοῖς πεπτικοῖς ὀργάνοις, γαστρί τε καὶ ἤπατι καὶ φλεψίν, ἐν οἶς ἄν προκατεργασθεὶς τρέφειν ἤδη δύναιτο τὸ σῶμα· πρὶν δὲ τῆς ἐν τούτοις μεταβολῆς ἐπιτυχεῖν οὐχ οἴόν τ' αὐτῷ τροφὴν ζώου γενέσθαι, κὰν εἰ δι' ὅλης ἡμέρας καὶ νυκτὸς ἐπικείμενος ἔξωθεν εἴη τῷ χρωτί.

¹⁴ Gal. De Temp. (1. 662, Kühn): ἄμα μὲν γὰρ ὅτι μεταβάλλεται καὶ ἀλλοιοῦται κατά τε τὴν γαστέρα πεττόμενα κἀν ταῖς φλεψὶν αἱματούμενα, πρὸς δὲ τούτοις καὶ διότι μὴ μένει καθ' ἕνα τόπον, ἀλλ' εἰς πολλὰ μερίζεται πάντη φερόμενα.

 $^{^{15}}$ Gal. De Temp. (1. 660, Kühn): τροφή γὰρ ἄπασα κατὰ τὸν ἑαυτῆς λόγον αὔξει τὸ τοῦ ζώου θερμόν.

¹⁶ Gal. De Temp. (1. 659-660, Kühn): οὕτως οὖν κἀν τοῖς ζώοις ὅσα τῶν ἐδεσμάτων, ἵν΄ ἐξομοιωθῆ τελέως καὶ θρέψη τὸ σῶμα, χρόνου δεῖται, ψῦχος μᾶλλον ἐπάγειν ἢ θάλπος ἐν τῷ παραυτίκα φαίνεται. θερμαίνει μὴν ἐν τῷ χρόνῳ καὶ ταῦτα, παραπλησίως τοῖς ἄλλοις ἐδέσμασιν, εἰ μόνον αὐτοῖς προσγένοιτο τὸ θρέψαι τὸ σῶμα.

¹⁷ Gal. De Temp. (1. 675, Kühn): καθ' ὅλου γὰρ ἐπειδὰν εἰς ταὐτὸν ἀλλήλοις ἥκοντα δύο σώματα διαμάχηταί τε καὶ στασιάζη πρὸς ἄλληλα περὶ τῆς ἀλλοιώσεως ἐν χρόνῳ πλείονι, δρᾶν καὶ πάσχειν ἑκάτερον αὐτῶν ἀναγκαῖόν ἐστιν.

In the last phase of the digestion mechanism alien substances are expelled. Whatever is not suitable for further use is removed – if the organism can do thiseither through excretion or through urinary system or through breathing through the porous of the skin¹⁸. Consequently a substance can be considered as food only when it can be assimilated to living organism and nourish it. Then and only then it is suitable and useful.

On the contrary, if a substance can not be assimilated to the living organism it can not be considered as food, but as a drug¹⁹. When a substance can not be assimilated to the body it is implied that it remains unchanged in it. The substance which prevailed is the drug that can either help or harm. In the second case, according to Galen, the substance is thought to be poison²⁰.

The "battle" for assimilation is the main part of the functional mechanism of drugs. The second part concerns the action of the winner-substance in the body. That substance according to its mixture may benefit the body having a therapeutic action according to the theory of "treatment with contraries to the symptom". That substance, according to its mixture, can help the body as in the example of the wild lettuce²². For instance, if its mixture is cold then it can certainly be used therapeutically for some organs whose mixture is unbalanced and more specifically hot. But if its mixture is too cold apart from equating the surplus heat, it can turn the organ's mixture into cold²³. In this way, if it is a cold poison and the organism will freeze to death. Finally, if a hot medicine remains unchanged by the organism it might rote the body's nature to death.

Therefore, a reference to the meaning of the drug is not possible unless the term is defined and clarified. The term must be differentiated by the meaning of food which is consumed using the same mechanism, the swallowing. A substance is characterized either as food or as a drug depending on the result of this process.

At this point we can give the definition of the drug, differentiating it at the same time from the term of food. Galen characterizes food, every substance or element that is dominated by the body and is assimilated to it, increasing its heat.

 $^{^{18}}$ Gal. De Temp. (1. 662, Kühn): ἔτι τε πρὸς τούτοις ὅτι διὰ ταχέων ἥ τε πέψις αὐτῶν γίγνεται καὶ ἡ διάκρισις, ὡς τὸ μὲν οἰκεῖον ἐξομοιωθῆναι, τὸ δὲ περιττὸν ἐν αὐτοῖς καὶ δριμὸ διὰ γαστρός θ' ἄμα καὶ οὔρων καὶ ἱδρώτων ἐκκριθῆναι.

 $^{^{19}}$ Gal. De Temp. (1. 656, Kühn): τὰ μὲν οὖν ὁμοιούμενα πάντη τροφαί, τὰ δ' ἄλλα σύμπαντα φάρμακα καλεῖται.

 $^{^{20}}$ Gal. De Temp. (1. 656, Kühn): διττή δὲ καὶ τούτων ἡ φύσις· ἢ γὰρ οἶάπερ ἐλήφθη διαμένοντα νικᾶ καὶ μεταβάλλει τὸ σῶμα, καθ' ὂν τρόπον ἐκεῖνο τὰ σιτία, καὶ πάντως ταῦτα τὰ φάρμακα δηλητήριά τε καὶ φθαρτικὰ τῆς τοῦ ζώου φύσεώς ἐστίν.

²¹ Τά ἐναντια τοῖς ἐναντίοις εἰσίν ἰήματα (latin transl. Contraria Contraribus cunantur)

 $^{^{22}}$ Gal. De Temp. (1. 678, Kühn): ώστε καὶ ἡ χρεία τῶν τοιούτων ἁπάντων διττὴ τοῖς ἰατροῖς ἐστι καὶ ὡς σιτίων καὶ ὡς φαρμάκων. φέρε γὰρ ὑπηλλάχθαι τινὶ τὴν ἀρίστην ἐν τῷ γαστρὶ κρᾶσιν ἐπὶ τὸ θερμότερον. οὖτος ἄχρι μὲν οὖ πέττει τὴν θριδακίνην, ἐμψυχθήσεται καὶ συμμετρίαν κτήσεται κράσεως· ἐπειδὰν δ' ἐξ αὐτῆς ἤδη τρέφηται, τὴν οὐσίαν αὐξήσει τῆς ἐμφύτου θερμασίας.

²³ Gal. De Temp. (1. 691, Kühn): οἶον εἰ ἄκρως ἡ διάθεσις θερμή, καὶ τὸ φάρμακον ἄκρως εἶναι ψυχρόν, εἰ δ' ὀλίγον ἀπολείποιτο τῆς ἀκρότητος ἡ διάθεσις, ὀλίγον χρὴ καὶ τὸ φάρμακον ἀπολείπεσθαι, κἂν εἰ πλέον ἀπέχοι τῆς ἄκρας θερμότητος ἡ διάθεσις, ἀνάλογον ἀπέχειν τῆς ἄκρας ψυχρότητος τὸ φάρμακον.

Galen notes "every living organism feeds on the suitable food. Suitable food for everyone is the substance that can be equated with the body it feeds"²⁴.

Drug, on the contrary, is whatever can not be assimilated to the living organism, no matter how that affects the body. In addition to these two categories there are some other substances that are both food and drugs. Firstly, they act as drugs and then they are assimilated by the organism and act like food, increasing the internal natural heat²⁵. In this case also, Galen uses the theory and the example to base his thought. Galen supports that a substance acts like drug during the digestion process and precisely for the time it is digested in the stomach before it is transformed to blood²⁶. In the last phase of digestion it is fully assimilated to the body and increases the internal natural heat of it.

It should be noted that Galen avoids the use of difficult reports and obscure examples. All his theoretical reports and examples are based on the cold-hot pair of opposites. The reason is obvious. His objective is to bring the researcher closer to his pharmacological theory. Studying Galen's third book the reader can feel that Galen concentrates on the trainee doctor.

In this case, he makes use of the wild lettuce example, which is naturally cold and is used to restore the ill-balanced mixture of the stomach which has turned from hot to cold. He says that when the wild lettuce affects more than it is affected in the body, it shows its power as a drug rather than when it is affected more than it affects when it shows the power of food.

DRUGS AND POISONS

After the definition Galen categorizes the drugs. According to him there are four groups²⁷:

- a) These which are immutable, unalterable and harm the body, they are poisons,
 - b) These which are alterable and harm the body, they are poisons,
 - c) These which are beneficial for the body and
- d) These affecting the body, but finally are assimilated to it and are nourishing it, that are drugs and food at the same time.

The poisons of the first category are naturally cold, like the example of opium, mandragora and the hemlock. These poisons are hostile substances for the human

²⁵ Gal. De Temp. (1. 677-678, Kühn): ώστ' εὐλόγως ἄμφω τοῖς τοιούτοις ἐδέσμασιν ὑπάρχει τό θ' ώς φαρμάκοις διατιθέναι τὰ σώμαθ' ἡμῶν καὶ τὸ τρέφειν, παρ' ὅλον μὲν τὸν χρόνον τῆς πέψεως ώς φαρμάκοις· ἡνίκα δ' ἤδη τρέφει τε καὶ τελέως ὁμοιοῦται, τότ' οὐκέτ' οὐδὲν ἡμᾶς ἀντιδρῶντα τὴν ἔμφυτον αὔξει θερμασίαν, ώς καὶ πρόσθεν εἴρηται.

 $^{^{24}}$ Gal. De Temp. (1. 655, Kühn): τῶν ζώων ἕκαστον οἰκείαις τρέφεται τροφαῖς· οἰκεία δ' ἐστὶν ἑκάστω τροφὴ πᾶν ὅ τι ἄν ἐξομοιωθῆναι δύνηται τῷ τρεφομένῳ σώματι.

²⁶ Gal. De Temp. (1. 682, Kühn): πάντα γὰρ ταῦτα καὶ τροφαὶ καὶ φάρμακα θερμά, πρὶν μὲν εἰς αἷμα μεταβαλεῖν, ἔτι γε πεττόμενα, φάρμακα, μεταβληθέντα δ' οὐκέτι μὲν φάρμακα.

²⁷ Gal. De Temp. (1. 656, Kühn): τὰ μὲν οὖν ὁμοιούμενα πάντη τροφαί, τὰ δ' ἄλλα σύμπαντα φάρμακα καλεῖται. διττὴ δὲ καὶ τούτων ἡ φύσις· ἢ γὰρ οἶάπερ ἐλήφθη διαμένοντα νικᾳ καὶ μεταβάλλει τὸ σῶμα, καθ' ὂν τρόπον ἐκεῖνο τὰ σιτία, καὶ πάντως ταῦτα τὰ φάρμακα δηλητήριά τε καὶ φθαρτικὰ τῆς τοῦ ζώου φύσεώς ἐστιν, ἢ μεταβολῆς ἀρχὴν παρὰ τοῦ σώματος λαβόντα σήπεται τοὐντεῦθεν ἤδη καὶ διαφθείρεται κἄπειτα συνδιασήπει τε καὶ συνδιαφθείρει τὸ σῶμα· δηλητήρια δ' ἐστὶν ἔτι καὶ ταῦτα. τρίτον δ' ἐπ' αὐτοῖς ἐστιν εἴδος φαρμάκων τῶν ἀντιθερμαινόντων μὲν τὸ σῶμα, κακὸν δ' οὐδὲν ἐργαζομένων καὶ τέταρτον, ὅσα καὶ ποιοῦντά τι καὶ πάσχοντα νικᾶται τῷ χρόνῳ καὶ τελέως ἐξομοιοῦται. συμπέπτωκε δὲ τούτοις ἄμα τε φαρμάκοις εἶναι καὶ τροφαῖς.

body since they can not be changed by the living organism and as a result they don't become one with it. The cold poisons alter the physical condition of the body according to theirs, in other words at first they freeze the body and later on they kill it.

On the contrary the poisons of the second category are naturally. Their functional mechanism is quite the same. They are unalterable and they are not assimilated to the body. However, in the next stage they have the opposite result. They multiply the internal heat of the body. According to Galen, hot poisons make use of the organism's heat and increase it excessively causing decay. In such a case the body's mixture turns into the poison's mixture²⁸.

Another categorization of the drugs that results according to the above is their differentiation in hot, cold, dry and wet. Although the categorization of the drugs in four subcategories seems to be simple, Galen makes more difficult the understanding and presentation of them as he introduces the Aristotelic ideas of "Everyeía" and "δυνάμει". Every drug either hot or cold and can be categorized according to its effectiveness. "Everyeía" means "active" while "δυνάμει" means "potentially". In other words, there are actively hot drugs or drugs that potentially become hot. The same goes for actively cold and potentially cold drugs, for actively dry and potentially dry drugs, for actively wet and potentially wet drugs.

Galen explains the idea of "active", supporting that drug has the quality either of hot or dry in an extreme degree²⁹. On the other hand he explains the idea of "potentially" saying that "nature reaches that point only if no external factor prevents it. All of these drugs (potentially) are not yet completely hot but are suitable for being and so. That why they are said to have the potential to become hot³⁰". The example of the wine is mentioned. The wine acts as a food and drug at the same time³¹. When wine comes in contact to the skin it acts not as hot drug but "potentially". It has the potential of being hot since the external contact doesn't heat the organism. But when wine is drunk, it becomes a hot drug and then a proper food.

Our latest observations so that Galen approaches quite effectively the modern theory of the functional mechanism of the drugs. But under no circumstances one could possibly think that Galen managed to accomplish such an unbelievable scientific achievement, since that would be beyond average measures of intelligence. Galen through all stages of writing "on mixtures" uses the reasoning and his huge medical experience; a statement that mentions quite a lot of time throughout his work. Experience and reasoning compose the basic methodology of his studies, researches and results, and through these his theories arise.

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 $^{^{28}}$ Gal. De Temp. (1. 656, Kühn): τὰ μὲν δὴ διαβιβρώσκοντα καὶ σήποντα καὶ τήκοντα τὴν τοῦ σώματος ἡμῶν φύσιν εἰκότως ὀνομάζεται δυνάμει θερμά, τὰ δ' αὖ ψύχοντα καὶ νεκροῦντα ψυχρά.

²⁹ Gal. De Temp. (1. 559, Kühn): "Οτι μὲν οὖν ἕκαστον τῶν ἐνεργεία θερμῶν καὶ ψυχρῶν καὶ ξηρῶν καὶ ὑγρῶν ἢ τῷ τὴν ἄκραν δεδέχθαι ποιότητα τοιοῦτον εἶναί φαμεν ἢ ἐπικρατήσει τινὸς ἐξ αὐτῶν ἢ πρὸς τὸ σύμμετρον ὁμογενὲς παραβάλλοντες ἢ πρὸς ὁτιοῦν τῶν ἐπιτυχόντων, ἔμπροσθεν εἴρηται.

³⁰ Gal. De Temp. (1. 647-648, Kühn): κυριώτατα μὲν οὖν ἐκεῖνα μόνα δυνάμει λέγομεν, ἐφ' ὧν ἡ φύσις αὐτὴ πρὸς τὸ τέλειον ἀφικνεῖται μηδενὸς τῶν ἔξωθεν ἐμποδὼν αὐτῆ γενομένου, ἤδη δὲ καὶ ὅσαι προσεχεῖς ὖλαι τῶν γιγνομένων εἰσίν.

³¹ Gal. De Temp. (1. 658-659, Kühn): Πάντ' οὖν ταῦτα τὰ φάρμακα θερμὰ μὲν οὔπω τελέως ἐστίν, ἐπιτηδειότατα μέντοι πρὸς τὸ γενέσθαι θερμὰ καὶ διὰ τοῦτο δυνάμει θερμὰ λέγεται. περὶ μὲν δὴ τούτων οὐδὲν ἄπορον, ἀλλ' οὐδὲ διὰ τί πινόμενος μὲν ὁ οἶνος ἱκανῶς θερμαίνει τὸ σῶμα, κατὰ δὲ τοῦ δέρματος ἐπιτιθέμενος οὐ θερμαίνει.

The key phrase that can really impress is the meaning of "speed of change" that connects time with the action of the drug. The exact phrase that he uses is "the same and the one and only criterion is the speed of change³²" but once more an explanation is needed since Galen means only the the speed at the start of action of the drug. An exception to that is the case of drug-food where the total time of action can only be measured indirectly; that time is the one needed for digestion in the stomach and can not have a specific measure and "action time" can not be certain.

Galen was an ordinary man of his era with specific abilities and weaknesses. What concerns him the most is the relation between time and action speed of the drug. He tries to understand and specify which drugs by nature are faster and not why they are faster. So according to his way of thinking drugs which are by nature extremely high in one of the qualities of hot, cold, dry and wet, but also are "active" drugs start to affect the organism in significantly less time than the "potentially" drugs.

While completing this research one can claim that Galen was the first one to try to understand the effectiveness of drugs. He avoided the simplistic description of drugs and the illnesses they are indicated for. Undoubtedly he made a huge step in favor of pharmacology, since he introduced it as an independent science. He teamed up pharmacology and humoral pathology giving to the first the prestige and above all the validity it needed. He was the first to accomplish to capture and describe a unique model of systematic pharmacology, overcoming the previous medical practice of just listing drugs. He made every possible effort to give reliable answers in the meaning of drug and its function. Since Galen the science of pharmacology made significant progress and moved through new scientific fields of knowledge, while steadily came to former way of being.

 $^{^{32}}$ Gal. De Temp. (1.669 , Kühn): κοινή δ' ἐπὶ πάντων ἡ κρίσις καὶ μία το τάχος τῆς ἀλλοιώσεως.

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