

Gut microbiota: One of the new frontiers for elucidating fundamentals of *Vipaka* in Ayurveda

Anagha Vishwas Ranade, Amey Shirolkar¹, Sharad Daulatrao Pawar²

Research Officer (Ayu), Department of Pharmacology, Regional Ayurved Institute for Fundamental Research, ¹Department of Biochemistry, National Centre for Cell Sciences, ²Research Officer (Pharmacology), Department of Pharmacology, Regional Ayurved Institute for Fundamental Research, Pune, Maharashtra, India

Abstract

With the increasing resurgence of Ayurvedic medicine in recent years, a lot of focus is laid on pharmacokinetics of herbs in arresting disease pathology. Ayurveda has enlisted some fundamentals in relation to drug pharmacokinetics, namely *Rasa* (perception), *Virya* (potency), *Vipaka* (postdigestive effect), *Guna* (properties), and *Prabhava* (special effect). In recent years, research has emphasized the role of gut microbiota in human health and metabolic processes. A thorough review was done to understand the role of microbiota in drug metabolism if any. The holistic mechanism of gut microbiota coincides to some extent, with the doctrines of Ayurveda in the context of pharmacodynamics and pharmacokinetics. This discussion is a thought put forth with an aim to elucidate the concept of *Vipaka vis-a-vis* gut microbiota functions.

Keywords: Gut microbiota, pharmacokinetics, *Vipaka*

Introduction

Gut microbiota is an organ by itself, with an extensive metabolic capability and functional plasticity.^[1] The gut microbiota maintains a symbiotic relationship with the gut mucosa in a healthy individual and execute substantial metabolic, immunological and gut protective functions.^[2] The gut microbiota obtains nutrients from host dietary components and shed epithelial cells.^[3]

Food components passing through the phase of mechanical and chemical digestion reach small intestine as well as endogenous compounds such as digestive enzymes and shed epithelial cells associated with mucus, entering the colon become available for fermentation by microbiota.^[4] Bacterial conversion of these compounds results in the liberation of various metabolites. Undigested carbohydrates and proteins constitute the major substrates at the disposal of the microbiota.^[5] Fermentation of these substrates results in the production of a range of metabolites including short-chain fatty acids (SCFAs), branched-chain fatty acids, ammonia, amines, phenolic compounds and gases, including hydrogen, methane, and hydrogen sulfide. In addition, the intestinal microbiota is involved in the production of B-complex group of vitamins, the

activation or inactivation of bioactive food components such as isoflavonoids and plant lignans, the conversion of prodrugs to their bioactive forms, and the transformation of bile acids and xenobiotics.^[6]

Human and microbial symbiosis possesses a close link with the diseases of different systems. Various chronic diseases such as inflammatory bowel disease, diabetes mellitus, metabolic syndrome, atherosclerosis, alcoholic liver disease, non-alcoholic fatty liver disease and cirrhosis have been associated with the human microbiota.^[7,8] These anomalies manifest due to the dysbiosis caused in microbiota, and thus, making them a novel therapeutic target.

There is growing evidence that the metabolism of polyphenols by the microbiota can influence their bioactivity; consequently, interindividual variation in microbial metabolism could have significance for the health benefits of phytochemicals.^[9] The best example is again the soy isoflavone and daidzein.

Address for correspondence: Dr. Sharad Daulatrao Pawar,
Regional Ayurved Institute for Fundamental Research, Pune - 411 038,
Maharashtra, India.
E-mail: sd_pawar@yahoo.com

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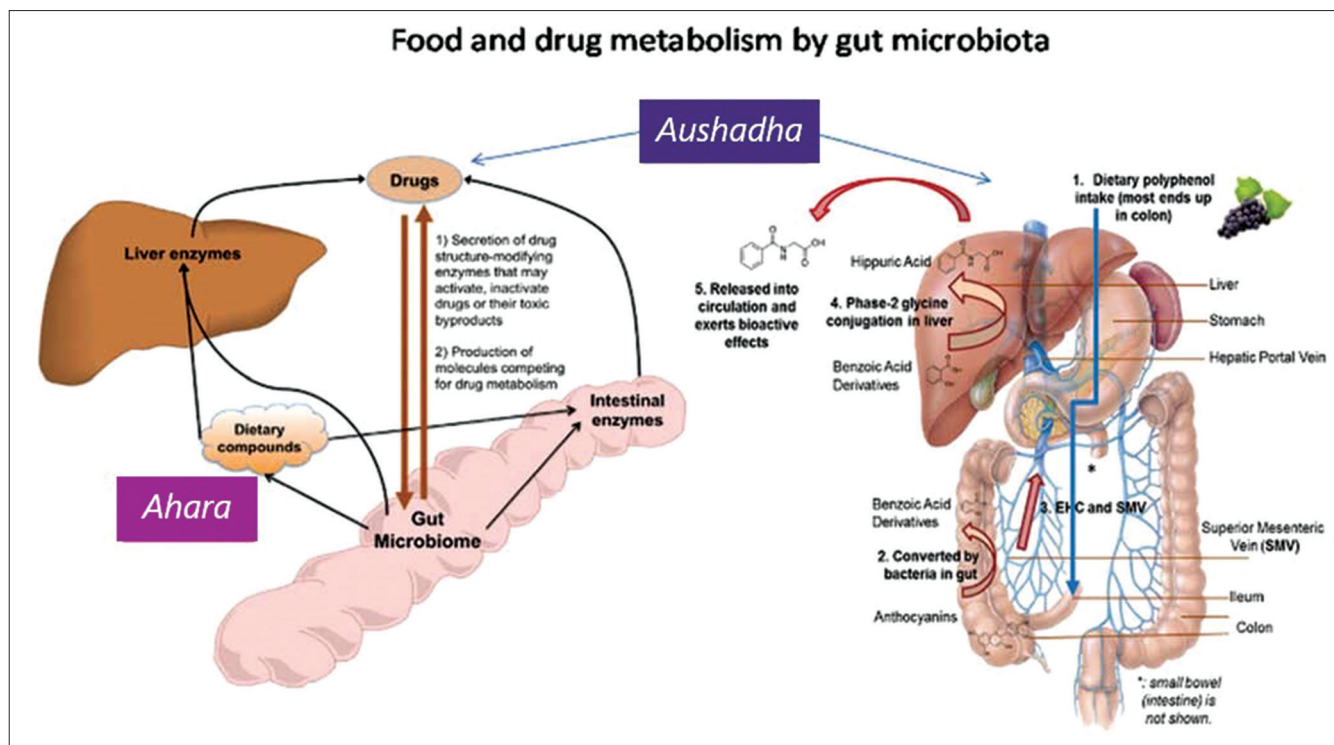


Figure 1: Overview of gut microbiota functions in food and drug metabolism

There is evidence that equol is more bioactive than its parent isoflavone in a range of areas including estrogenic and antiestrogenic activity, antioxidant capacity and potential anticancer effects.^[10] The gut microbiota contributes readily in interpersonal variation in drug response in humans.^[11,12]

Fundamentals of *Vipaka*

In *Ayurveda*, pharmacological effect of *Ausadha Dravya* (drug) has been explained in *Dravyaguna* on the basis of the theory of *Rasapanchaka*.^[13] It comprises *Rasa* (perception), *Vipaka* (postdigestion effect), *Guna* (quality), *Virya* (potency) and *Prabhava* (special effect).^[14] These components form an integral part of Ayurvedic pharmacodynamics and pharmacokinetics. The seers have stated that a drug exhibits its action either by its *Rasa*, *Guna*, *Vipaka*, *Virya* or *Prabhava*.^[15]

Each of these five ascriptions contributes individually in deciding the fate of *Dravya* (i.e., medicine or food) without disturbing the collective penta-equilibrium. The fundamentals of *Vipaka* are closely associated with the post assimilation phase of digestion in humans.

Ayurveda describes the physiology of digestion using three stages rightly known as *Avasthapaka*,^[16] wherein sequential changes in the chemical and mechanical nature of *Dravya* are well documented.

The *Avasthapaka* basically consists of three phases as per Charaka, namely *Madhura* (sweet), *Amla* (sour) and *Katu* (pungent). The correlation between *Avasthapaka* and phases of digestion has been reported.^[17]

Madhura Avasthapaka

It commences as soon as the food comprising *Shadrasa* (six tastes) comes in contact with *Bodhaka Kapha* and continues up to *Amashaya* (fundus part of stomach). In this process, thin and frothy *Kapha* is generated. It is often correlated with the breakdown of starch by salivary amylase and partial digestion in the fundal part of the stomach, where polysaccharides are broken down to monosaccharides.

Amlavasthapaka

Later, the partially digested (*Pakva* and *Apakva*) food comes in contact with *Amashaya* (pyloric part of stomach) with the environment consisting of HCl that facilitates digestion of proteins, and the resultant acidified chyme (*Vidagdha*) is propelled into duodenum ahead, where *Achha Pitta* which intermittent secretion in *Grahani* (duodenum) during *Paka* (digestion) is produced which is often correlated with secretion of bile.

Katuavasthapaka

When this food byproduct reaches *Pakvashaya* (large intestine), it gets further metabolized and hydrolyzed by the *Agni* (metabolic energy), and it takes a bolus form (*Paripindita*), resulting in formation pungent taste. This stimulates *Vata Dosha*. This phase is often equated with the last stage of digestion occurring in the colon along with formation of indole, skatole and excretory products.

A lucid discrimination has been mentioned between *Vipaka* and *Avasthapaka* although both have numerical similarities by Charaka.^[18] Sushruta has quoted two types of *Vipaka* based on

the physical properties (*Guna*).^[19] It stresses more on structural and functional relationships related to *Panchamahabhuta* configuration.

The *Vipaka* is the final transformation of food, whereas *Avasthapaka* is the initial phase. *Vipaka* commences only after the *Avasthapaka* has ceased. This has been denoted in the Chakrapani commentary in Ca.Ci. 15/9–11. The term *Bhinna Kala* (time factor) denotes that these two stages are different.^[18] The actual vitiation of *Dosha* which, in turn, intimates the end of metabolism (*Rasa Mala Viveka*)^[18] is termed as *Vipaka*. The factors that determine the *Vipaka* are *Dosha*, *Mala* (fecal matter and urine), and the effect on *Shukradhatu* which is the last tissue in sequential nutrition as per Ayurveda.^[20] Thus, *Vipaka* is closely associated with secretion and absorption functions after the mechanical and chemical digestion. It is quoted as *Karma Nishthaya*, that is, it manifests its properties at the end of complete digestion of food/drug.^[21,22] Thus, it suggests that *Vipaka* is an entity which results in food/drug metabolism for tissue nutrition or cellular nutrition. Three specific *Vipaka* are themselves responsible for some peculiar action (food/drug metabolism at different stages) as per classics.

The studies^[23-26] that have been carried out abiding by the concept of *Vipaka* includes very few preclinical and clinical documentation that focus on the “*Karma Nishthaya*” function of *Vipaka*, which is partially valid. It rightly denotes the impact of drug on *Mala Karma*, but it is not efficient in validating the metabolism aspects of the drug. These do not wholly suffice the concept as *Mala* is not the only criterion for deciding *Vipaka*.

Gut microbiota vis-a-vis *Vipaka*

Vipaka commonly referred to as “*Karma Nishthaya*,” that is, “postdigestive irreversible process” is closely associated with biotransformation of drug/food caused by microbiota. Bhadanta Nagarjuna has stated that *Parinam Lakshano Vipaka* which again points towards biotransformation.^[27] In Ayurveda, the term “*Vi*” is *Vishishtha*, that is, specific, and “*Paka*” refers to function assigned to *Agni* (metabolic energy).^[28] These microflora themselves are sources of *Agni* which reside in *Mahasrotasa* (gastrointestinal tract) and are responsible for the metabolism of drug. Gut microflora in total exhibits certain specificity in ultimate production of SCFAs and other nutrients depending on the quantity and nature of the diet and medicines. Similarly, the *Madhura*, *Amla* and *Katu Vipaka* of drug (food/medicine) have been denoted to possess qualitative degree (*Taratama Bhava*)^[29] depending on the nature of the drug consumed which manifests in *Karma* (action) of the drug. The overview of gut microbiota functions in food and drug metabolism vis-a-vis *Vipaka* has been depicted in Figure 1.

Evidence states that the intestinal microbiota may play an important role in mediating the metabolism and enhancement of bioactivity of many herbs such as ginseng.^[30] Gut microbiota surely plays a role in decreasing as well as increasing drug activity.^[31]

The conventional approach of drug discovery is to isolate pure bioactive molecules from the medicinal plant extracts and study their pharmacokinetics and metabolism. This is a hindrance to the concept of whole-drug usage in Ayurveda. Basically, the metabolism of herbal medicines is very complex in comparison to single isolates. The above-mentioned concept of *Vipaka* along with gut microbial interactions with medicinal plants can certainly give new insights into pathway of drug discovery. Exploratory research in this line can surely aid in scientific validation of *Vipaka* which is one of the doctrines of *Dravyaguna*.

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Conflicts of interest

There are no conflicts of interest.

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