Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol.14, Issue 33s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Anupana: The Silent Architect Of Ayurvedic Pharmacodynamics

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Cite this paper as: : Dr. Noor Fathima, Dr. Spandana M, Dr. G S Sahana, Dr. Haripriya S,. Dr. Raghunath M , Dr. Anil Kumar K M , Chethan Kumar B G (2025) Anupana: The Silent Architect Of Ayurvedic Pharmacodynamics..Journal of Neonatal Surgery, 14, (33s) 330-338

ABSTRACT

Ayurveda, the oldest living Medical Science, holds timeless knowledge that still guides healing today. It recognizes that treatment must suit the individual in the personalized approach and Anupana becomes an inseparable part of therapy. Anupana, the adjuvant administered along with or after medicine, is a classical Ayurvedic concept with potential implications for therapeutic precision. Despite extensive textual descriptions, its mechanistic and translational relevance remains underexplored.

Keywords: Anupana, Bioavailability, Yogavahi, Phytopharmaceutical absorption

1. INTRODUCTION

Ayurveda, a comprehensive medical system that conceptualizes health and disease through an integrated understanding of biological balance, lifestyle, and therapeutic interventions. Although its foundational doctrines were articulated millennia ago, they continue to be critically examined in contemporary research for their translational relevance and clinical applicability. The objective of Ayurveda to preserve health in the healthy and to alleviate disease in the afflicted underscores its preventive and curative dimensions. Within this framework, Anupana represents a strategically significant yet underexplored concept, referring to the adjuvant substance administered along with a medicine or diet. Beyond its traditional description, Anupana can be viewed as a modulator of drug action, influencing assimilation, distribution, and therapeutic response. Its role as a synergistic and context specific adjunct positions Anupana as a scientifically pertinent component of Ayurvedic pharmacotherapeutics, warranting systematic evaluation in the light of modern biomedical understanding. Ayurveda adopts a personalized approach to the administration of ahara and aushada, employing specific Anupana based on factors such as dosha, kala, vyadhi avastha etc administered along with or subsequent to food and medication, Anupana facilitates enhanced drug assimilation and therapeutic efficacy. Conceptualized as Yogavahi(1) it augments the action of the primary drug by improving oral bioavailability, minimizing adverse effects, and directing the active principles to the intended site of action. Hence, the rational selection of Anupana is essential to optimize outcomes across individuals and clinical conditions.

2. DEFINING THE VEHICLE

अन्नदनुपश्चात् पीयते इत्यनुपानम् I (डल्हण सु.सू ४३/४१९)

According to *Sushruta samhitha Anupana* is the liquid consumed immediately after food or along with it..

औषध भक्षणोपरि यत्पीतं तदनुपानममत्यर्थ: I (आढमल्ल शा.स.म ६/४-५) *Adamalla* defines *anupana* as the vehicle used after administration of main drug

तत्तद् ि◌ोच्यन भैषज्यं भेषजस्यानुमपयते यच्च सहायकारि स्याद् अनुपानं तद् उच्यते I

(ि◌सतिंमिमण)

Anupana is the one that is taken along with main drug that helps in easy disintegration, absorption and uniform distribution of medicine all over the body

CLASSICAL SIMILE THAT REVEAL *ANUPANA'S*

PURPOSE

य◌ा जलितं तैलं तत्क्षणादेव सपथमत I त◌ा भैषज्यमअङ्गेषु प्रसपथत्यनुपानत: I इमत

I

Adamalla is of the opinion that similar to how an oil drop spreads rapidly over the surface of water, the drug when given with appropriate *anupana* reaches the target site thereby enhances the bioavailability and promotes easy absorption

GUNAS THAT SHAPE *ANUPANA*

यदाहि ि◌ुणै: पानं वीपितं तमदष्यते I

अन्नपानं धातूनां दृष्टं यन्न मविोमध च II (च.सू २७/३१९)

Anupana should have qualities similar to *Deha Dhatus* and opposite qualities to food consumed.

CLASSICAL CATEGORIES

BASED ON TIME OF ADMINITSTARTION

Aadipana	Before meal	*Karshana*	*Kshoudra* with luke warm water
Madhyapana	During Meal	*Sthapana*	*Takra* with *Ahara* in *Agnimandya/Arshas*
Anthapana	After Meal	*Brumhana*	*Ksheera/Mamsarasa*
Sahapana	With *Ahara/Aushadha*	*Yogavahi*	*Yashtimadhu churna* with *ksheera*

BASED ON THE FORM

Drava	*Kaishora guggulu* with *Manjishtadi kashaya* in *Vata rakta*
Shushka	*Pippali churna* in *Pleeha roga*

ACCORDING TO RAJA NIGHANTU

Kramana	*Anupana* administered after a certain time	*Rasa Sindhoora* with *Tulasi swarasa* in *Nava jwara*

Pachaana	*Anupana* is given along with *Ahara/Aushada*	*Hinguvashtaka churna* with *Grutha*

BASED ON USAGE

Aharaupayogi	*Mudgadi Dhanya* to be comsumed with *Mamsa rasa*
Aushadhaupayogi	*Indukantha grutha* with *guduchi swarsa*

UNLOCKING DRUG DESTINY: *ANUPANA'S*

MECHANISTIC ROLE

Therapeutic adjuvants are defined as constituents added to the preliminary drug in order to improve target specific treatments. They are used alongside primary therapies to enhance their effectiveness.

Adjuvants can be defined as substances that increase potency of a formulation when added/mixed to it.

Purpose of therapeutic adjuvants is to

Enhance efficacy

Reduce the rate of recurrence

Improve target specific protocols

The recommendation of medicine is incomplete in Ayurveda without the practice of *Anupana*.

Bio-Enhancing activity of *Anupana*[2]

The concept of Bioavailability enhancer is new to the modern system of medicine. Basically, this concept originated in Ayurveda and is being used in this system of medicine since centuries. Bio-enhancers augment the bioavailability or biological activity of drugs when co- administered with principal drug at low doses.

This bio-enhancement:

⌛ Leads to reduction in therapeutic dose of principal drug

⌛ Reducing the possibilities of toxicity and side effects of drug

⌛ Potentiating the efficacy by reducing the resistance

⌛ Decreasing the requirement of raw material for drug manufacture

⌛ Ultimately benefitting to the World economy by reducing the treatment cost. [3][4]

Yogavahi action of *Anupana*

The concept of *Yogavahi* for enhancing bioavailability is being used in Ayurveda since time immemorial. A very common example of *Yogavahi* in Ayurveda includes *Pippali* (P. longum) and *Maricha* (P. nigrum), which contain an important active compound named "piperine" (1-piperonyl piperidine) which is responsible for

bio-enhancing effect.

It has been found that piperine's bioavailability-enhancing property may be attributed to increased absorption, which may be due to alteration in membrane lipid dynamics and change in the conformation of enzymes in the intestine.

Piperine has been demonstrated to increase the serum levels and lengthen the serum half-lives of some nutritional substances, such as coenzyme Q10 and beta-carotene. On the basis of traditional use, honey is considered the best *Yogavahi* by many authors in *Ayurveda.*

Anupana in terms of external administration

There is a considerable interest in the delivery of drugs through skin into the systemic circulation and for local effect.

However, the outermost layer of the human skin, stratum corneum, presents a formidable barrier and also interferes with the absorption of topical therapeutic drugs, and drug penetration, thereby reducing bioavailability.

Skin penetration enhancement is achieved through modification of stratum corneum by hydration/chemical enhancers action on the structure of the stratum corneum lipids and keratin partitioning and solubility effects. Numerous vehicles and penetration enhancers have been synthesized to increase transdermal delivery of drugs, such as

alcohols, azone, esters, glycols, fatty acids, pyrrolidone's, sulfoxides, and terpenes.

In Ayurveda, use of *Lavana* (salt) along with oil for external application has been mentioned as if *Lavana* is mixed with oil, it helps to open the Srotas (microchannels of the body) due to its Sukshma and penetrating power of the oil and thus, ultimately results in the potentiation of efficacy.

Similarly, some other drugs are also described for the same purpose when used externally with principal drugs such as honey, Ghrita, and oil.

Factors affecting selection of *Anupana*

Absorption of Drug:

Cell Membrane Barrier: Absorption is the movement of drug from its site of administration into the circulation. It depends on various factors like aqueous solubility, concentration, area of absorbing surface, vascularity of the absorbing surface and its route of administration and ayurvedic drugs are mostly used orally. The effective barrier to orally administered drugs is the epithelial lining of the gastrointestinal tract which is lipoidal. All pharmacokinetic processes involve transport of the drug across biological membranes and biological membranes is a bilayer of phospholipid and cholesterol molecules and those drugs which are lipid soluble travels more easily across cells. Nonionised lipid soluble drugs are readily absorbed from stomach as well as intestine at rates proportional to their lipid: water partition coefficient [(5)] Mostly drugs are transported across the membranes by passive diffusion. The rate of lipid soluble drugs is more as compared to water e.g *Narayana churna* is given with *takra* as *anupana* in *udararoga* which is fatty in nature. A study has been done which shows that says that the *takra* is composed of lipids in it. [(6)]

Ph of Drugs: Acidic drugs are predominantly unionised in the acid gastric juice and are absorbed from stomach while alkaline drugs are largely ionised and are absorbed only on reaching the small intestine. However, even for acidic drugs absorption from stomach is slower because the mucosa is thick, covered with mucus and the surface area is small. Thus, faster gastric emptying accelerates drug absorption in general. In terms of pH, it is said that a drug becomes more lipid soluble in a solution which has the same pH as that of the drug. Thus increases the solubility of the drugs because a study has been done that whether the drugs are *ushna* or *sheeta virya* they are weakly or strongly acidic in nature.

So, if we take an example of *narayana churna* in *gulma roga* it is given with *badarambu* so both of these are acidic in nature. [(7)]

Particle Size of Drugs: Other than the Bhasma and liquid preparations in most of the dosage forms of ayurvedic drugs particle size are not so fine viz. *Vati*, *Guggulu, Churna, Kalka*. Absorption of coarse powder is less than absorption of fine powder because the dissolution is a surface phenomenon therefore particle size of the drug in solid dosage form governs rate of dissolution and in turn rate of absorption.

Filtration: It is the passage of drugs through aqueous pores in the membrane or through paracellular spaces. Lipid insoluble drugs across the biological membranes if their molecular size is smaller than the diameter of the pores.

It has been found in some studies that the dissolution with liquid or in other terms *anupana* decreases the particle size of the molecules of drug, facilitates its transport and hence increases the bioavailability of drugs

Bioavailabity: It is lower for lower ingestion because firstly the drug may be incompletely absorbed and secondly the absorbed drug may undergo first pass metabolism in intestinal wall or liver or be excreted in bile. Hence absorption is directly proportional to bioavailability. [(8)]

Intensity of Response: It is related to the concentration of the drug at the site of action which in turn is dependent on its pharmacokinetic properties. All these factors are increased due to mixing of *anupana* with the drug because solubility increases the concentration of drug and lower particle size resulting from dissolution also increases the area of absorption of drug which ultimately increases the absorption of drug and governs the distribution of drug in the body [(9)]

CLINICAL WINDOWS INTO *ANUPANA'S* POWER

A case study conducted on a 43-year-old overweight female diagnosed with Grade II non-alcoholic fatty liver disease (NAFLD) with altered liver function tests and characteristic symptoms such as right hypochondriac pain, fatigue, abdominal heaviness, and incomplete bowel evacuation .

The patient was treated for two months with *Rohitaka Abhaya Kwatha*, administered along with *Pippali churna* as *Anupana*,

followed by dietary regulation for three additional months .

The results showed marked symptomatic relief, improvement in BMI, normalization of liver function parameters, and complete resolution of fatty infiltration on ultrasonography after five months .

The study highlights that the formulation effectively improved *Agni*, reduced *Kapha–Meda dushti*, and cleared *srotorodha* at the hepatic level, addressing the core pathology of NAFLD

The *Anupana Pippali churna* played a crucial role by enhancing drug bioavailability, stimulating digestion and metabolism, and exerting hepatoprotective and anti-inflammatory actions .

Overall, the case demonstrates that the use of an appropriate *Anupana* significantly augments therapeutic efficacy, making the intervention both simple and cost-effective in managing NAFLD [(10)]

An open-label, single-arm clinical study conducted on 28 patients of *Apabahuka* (frozen shoulder) to evaluate the effectiveness of *Vatagajankusha Rasa* administered with *Pippali Churna* and *Manjishta Kwatha* as *Anupana* .

The intervention was given twice daily for 7 days, and both subjective *parameters (Amsa Sandhi Shoola, Bahupraspandita Hara)* and objective parameters (range of motion and Constant– Murley score) were assessed .

The results showed statistically significant reduction in pain and stiffness, along with marked improvement in shoulder movements such as flexion, abduction, internal and external rotation ($p < 0.005$) . There was also a highly significant improvement in functional ability, as reflected by an increase in the Constant– Murley score after treatment .

The *Anupana* played a crucial role, where *Pippali Churna* enhanced *Deepana–Pachana*, drug absorption, and *Yogavahi* action, facilitating rapid penetration of the formulation .

Manjishta Kwatha as *Anupana* contributed anti-inflammatory, circulatory, and *Shothahara* effects, supporting tissue nourishment and faster recovery of shoulder mobility .

Overall, the study demonstrates that the use of an appropriate *Anupana* significantly potentiated the therapeutic efficacy of *Vatagajankusha Rasa* in the management of frozen shoulder [(11)]

A randomized controlled experimental study protocol designed to evaluate the concept of *Anupana* as a bioavailability enhancer, with special reference to *Saindhava Lavana* used along with *Haritaki*

Kwatha in healthy volunteers .

The study proposes enrolling 60 healthy volunteers, divided into two groups—one receiving *Haritaki Kwatha* alone and the other receiving *Haritaki Kwatha* with *Saindhava Lavana* as *Anupana* .

Blood samples are planned to be collected at predetermined time intervals up to 360 minutes to assess phenolic compounds in serum using HPLC, which serve as objective markers of bioavailability . The primary objective is to compare the extent and rate of absorption of *Haritaki's* active constituents with and without *Anupana* .The outcome of the study was that *Saindhava Lavana* as Anupana significantly enhance the bioavailability of *Haritaki* compared to its administration alone .

Anupana acts as a *Yogavahi* or catalytic agent, facilitating rapid systemic distribution, improving absorption, and helping maintain effective drug concentration in circulation.[(12)]

A Study on *Anupana* w.s.r. to the Role of *Ghrita* in *Vataja Kasa* was conducted as a comparative single-blind clinical study with a pre- and post-test design on patients suffering from *Vataja Kasa*.

Thirty patients were divided into three groups (A, B, and C), each receiving *Vidangadi Churna* after food, administered respectively with *Ushna Jala, Ghrita,* and without any *Anupana*.

The study aimed to evaluate how different *Anupana* influence the therapeutic efficacy of the same formulation.

The results demonstrated that Group B, which received *Ghrita as Anupana*, showed superior clinical improvement compared to the other two groups.

This indicates that *Ghrita* significantly enhanced symptom relief in

Vataja Kasa when compared to *Ushna Jala* or no *Anupana*.

The study interpretation explains that *Anupana* functions both as *Sahapana* (co-administration) and *Pashchatpana* (post-administration), aiding drug delivery and action.The study supports the classical Ayurvedic concept that *Ghrita* acts as an effective *Yogavahi* and bioavailability enhancer, potentiating the therapeutic outcome of the main drug in *Vataja Kasa*[(13)]

COCRYSTALS AS A TECHNOLOGICAL PARALLEL TO *ANUPANA*

The physicochemical properties, such as the stability, particle size, powder flowability, taste, hygroscopicity, solubility and

compatibility, of active pharmaceutical ingredients (APIs) are critical attributes that impact the therapeutical effectiveness and manufacturing cost of solid dosage forms. [14] In oral drug delivery, gastrointestinal absorption largely depends on the solubility and dissolution rate of the drug.

However, almost 90% of new chemical entities and nearly 40% of marketed drugs belong to BCS class II and IV, exhibiting poor aqueous solubility and low bioavailability. These limitations restrict GI absorption and hinder clinical efficacy. As the solid-state properties of drugs strongly influence dissolution, there is a growing need for approaches that enhance solubility without changing the drug molecule itself. Pharmaceutical cocrystals offer such a strategy by pairing the API with a suitable coformer through non-covalent interactions, solubility, dissolution, and bioavailability can be improved while preserving the intrinsic properties and efficacy of the drug. Pharmaceutical cocrystals are multicomponent systems in which at least one component is an active pharmaceutical ingredient and the others are pharmaceutically acceptable ingredients. Cocrystallization of a drug substance with a coformer is a promising and emerging

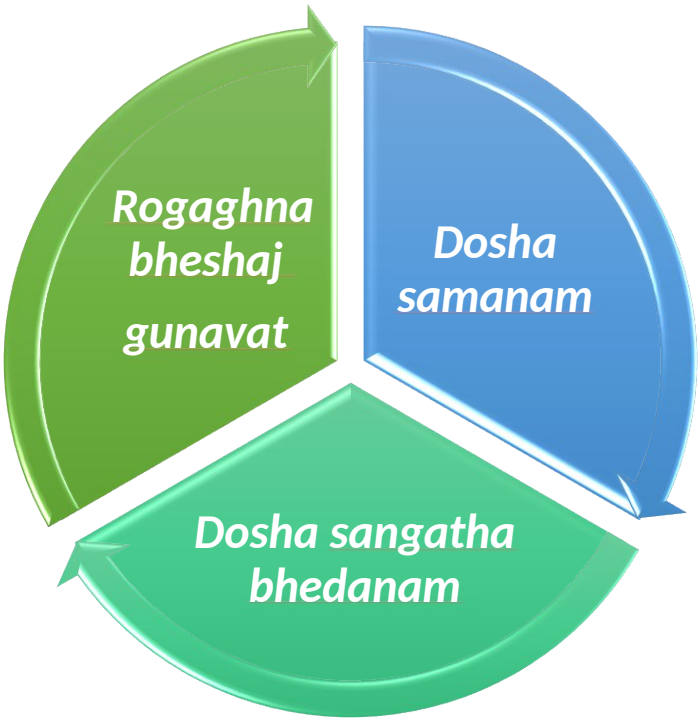
approach to improve the performance of pharmaceuticals, such as solubility, dissolution profile, pharmacokinetics and stability. In the last decade, cocrystallization has shown its potential to improve in vivo performance by enhancing the solubility, and bioavailability of poorly water-soluble drugs [15-19]. This strategy is especially suitable for drugs unable to form salts due to the lack of ionizable functional groups. Glibenclamide (GCM) is a BCS class II drug for the treatment of type II (noninsulin-dependent) diabetes; it is a second-generation sulfonyl urea that has low solubility but high permeability. The plasma glucose levels of the rats in different systems were evaluated in protein-free plasma by enzymatic glucose oxidase peroxidase after 7 days of oral administration. The maximum value of glucose reduction was up to 93.68% for glibenclamide–succinic acid cocrystal (GCM–SA), 78.46% for glibenclamide–nicotinic acid cocrystal (GCM–NA), 69.57% for glibenclamide–hippuric acid cocrystal (GCM–HA), 53.68% for glibenclamide–theophylline cocrystal (GCM–TP) and 40.68% for GCM [20]

Just as modern pharmaceutical science seeks to enhance bioavailability through cocrystallization where a coformer interacts with the API without altering its chemical structure, *Ayurveda* articulated a parallel concept centuries ago in the form of *Anupana*. *Anupana* referring to the vehicle taken along with medicine to potentiate its absorption, distribution, and therapeutic efficiency.

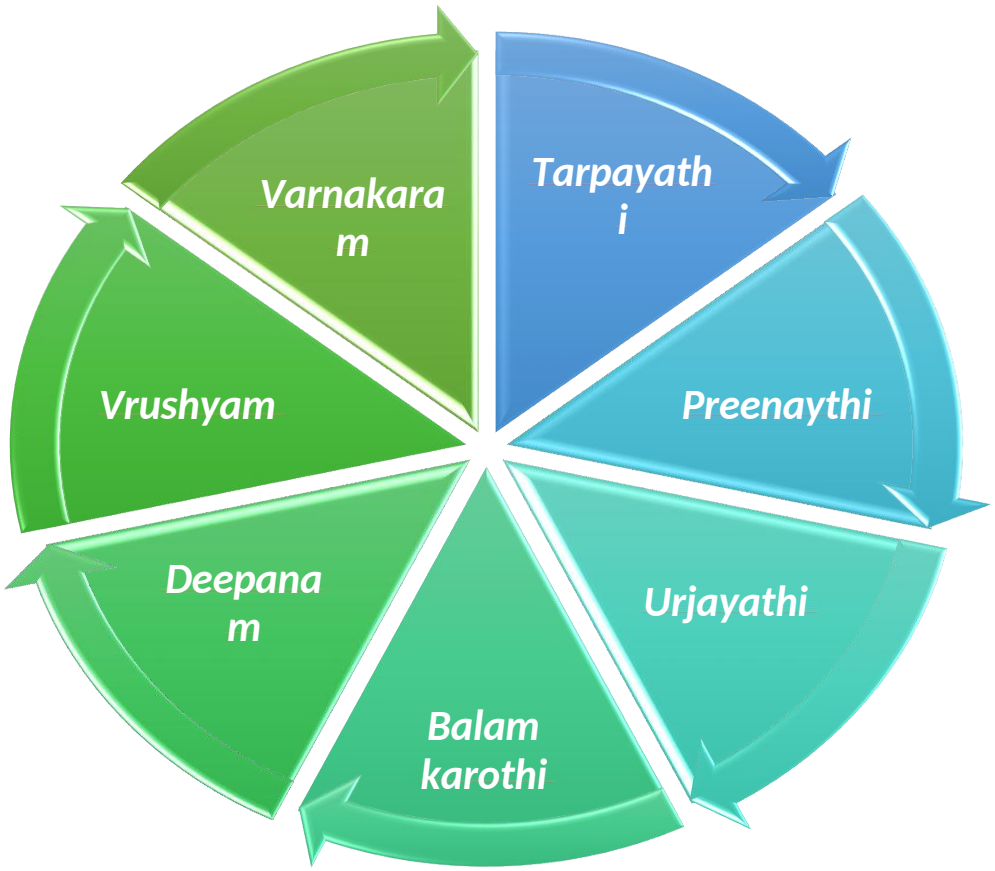
Importantly, it does so without modifying the intrinsic chemistry of the plant molecule or the polyherbal formulation, instead optimizing its delivery through suitable media such as *ghṛitha, madhu, takra, ushna jala* etc based on *doṣa, kala, roga rogi avastha*. Thus, emerging technologies like pharmaceutical cocrystals echo the ancient

Ayurvedic understanding that judicious combination with an appropriate companion substance can enhance solubility, absorption, and therapeutic outcomes while preserving core drug identity

Mode of action on *Aushada*



Mode of action on *Roga*



Mode of action on *Rogi*

3. CONCLUSION

The present review establishes that *Anupana* is not merely an ancillary drug vehicle, but a decisive contributor to absorption, distribution, metabolism, and therapeutic outcome as envisioned in classical *Ayurveda*. Its *guṇa* based selection, *yogavahi* potential, and relevance across both internal and external routes indicate that rational co-administration can optimize pharmacokinetics, minimize adverse effects, and potentiate efficacy through reduced dosage requirements. Clinical and mechanistic evidence, suggests that *Anupana* acts as a natural bioavailability enhancer without altering chemical identity an approach foundational to personalized medicine. To bridge traditional insights with present day pharmaceutics, future research must emphasize physicochemical standardization, pharmacokinetic modeling, and rigorous clinical trials exploring *Anupana*–drug interactions. Such efforts will not only validate the ancient wisdom of *Anupana* but also expand its applicability as a sustainable and scientifically grounded adjuvant in modern integrative therapeutics.

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