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# *DHANADANAYANADI KASHAYA* IN NEUROLOGICAL DISORDERS: A SYSTEMATIC REVIEW OF PHARMACODYNAMICS, PHYTOCHEMISTRY, AND MULTI-TARGET MECHANISMS

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## ABSTRACT

**Background**: *Dhanadanayanadi Kashaya* is a classical polyherbal decoction documented in the *Sahasrayoga (Kashaya Prakarana)*, traditionally indicated for the management of *Vata rogas* (neurological and neuromuscular disorders), specifically *Ardita* (facial paralysis/Bell's palsy) and *Akshepaka* (convulsive disorders or tremors). **Aim**: This review systematically analyses the classical Ayurvedic pharmacodynamics (*Rasa, Guna, Virya, Vipaka, Doshakarma*) of its 14 individual herbal components, delineates their known chemical profiles, maps their pharmacokinetic behaviour (ADME), and proposes an integrative multi-target mechanism of action. **Results**: The formulation demonstrates a predominant combination of *Katu* (pungent), *Tikta* (bitter), and *Kashaya* (astringent) *Rasas*; *Ushna* (hot potency) *Virya*; and *Laghu* (light), *Ruksha* (dry), *Tikshna* (sharp), and *Sukshma* (subtle) *Gunas*. Systemic integration of these properties resolves *Srotorodha* (microchannel blockages) and pacifies *Avarana Vata* (obstructed neural signalling). Concurrently, modern pharmacological data indicate that the bioactive constituents (e.g., piperine, gingerols, bonducin, plumbagin, alpha\beta-asarone) exert significant neuroprotective, anti-neuroinflammatory, and bio-enhancing effects. **Conclusion**: *Dhanadanayanadi Kashaya* acts through a bidirectional axis: resolving metabolic deficits (*Agnimandya* and *Ama*) at the gut level while simultaneously crossing the blood-brain barrier to attenuate neuroinflammatory damage and stabilise synaptic transmission.

**KEYWORDS**: *Dhanadanayanadi Kashaya*, *Akshepaka*, *Ardita*, *Vata roga*, Neurological disorders, Neuroprotection.

## INTRODUCTION

*Ayurveda*, being the traditional system of medicine, is known as the 'Science of Life'. In this science, everything in the universe is said to be medicine when it is used in the proper form and dose. The science is based on various theories, such as *Panchamahabhuta sidhanta*, *Tridosha sidhanta*, etc. The *tridosha*, namely *Vata*, *Pitta*, and *Kapha*, balance health when in a normal state, but cause diseases on imbalance. This imbalance, leading to diseases, can occur due to exogenous and endogenous factors. Along with an understanding of the disease, it is important to explore various formulations and their mode of action for an Ayurvedic physician.

*Dhanadanayanadi Kashaya* is one such formulation mentioned in *Sahasrayoga*, *Kashaya prakarana* for *Vata rogas* like *Arditha* and *akshepaka*. This article presents an overview of the pharmacological properties of individual components of this polyherbal combination, their collective effect and probable mode of action.

## MATERIALS AND METHODS

### MATERIALS

- Classical Ayurvedic textbooks
- Ayurveda Pharmacopoeia of India
- Articles published in PUBMED, IJRAP, KJA ….
- Lexicons

**Method:** Conceptual review.

**Table I: Ingredients Of Formulation.**

| No | Drugs | Botanical name | Family | Parts used |
|---|---|---|---|---|
| 1 | *Dhanada nayana* | *Caesalpinia bonduc* | Caesalpinaceae | Seeds |
| 2 | *Shunti* | *Zingiber officinale* | Zingiberaceae | Dried rhizome |
| 3 | *Sigru* | *Moringa oleifera* | Moringaceae | Root bark, leaves, seeds |
| 4 | *Rasna* | *Alpinia galanga* | Zingiberaceae | Root and leaves |
| 5 | *Ugragandha* | *Acorus calamus* | Araceae | Rhizome |
| 6 | *Varuna* | *Crataeva nurvala* | Capparaceae | Stem bark |
| 7 | *Lasuna* | *Allium sativum* | Liliaceae | Bulb (cloves) |
| 8 | *Krishna* | *Piper longum* | Piperaceae | Fruit |
| 9 | *Chitraka* | *Plumbago zeylanica* | Plumbaginaceae | Root |
| 10 | *Eranda* | *Ricinus communis* | Euphorbiaceae | Root, root bark, seeds, leaves |
| 11 | *Suradaru* | *Cedrus deodara* | Pinaceae | Heartwood |
| 12 | *Ghana* | *Cyperus rotundus* | Cyperaceae | Rhizome/Tuber |
| 13 | *Pathya* | *Terminalia chebula* | Combretaceae | Dried fruit |
| 14 | *Berbara* | *Clerodendron serratum* | Verbenaceae | Root |

*Dhanadanayanadi Kashaya* comprises 14 ingredients: *Dhanadanayana, Shunti, sigru, rasna, ugragandha, varuna, lasuna, krishna, Chitrakamula, Eranda, suradaru, khana, pathya, berbara.*

## PROPERTIES OF INGREDIENTS

**1. *Dhanadanayana*[1]**

- ***Rasa:*** *Tikta, Katu, Kashaya*
- ***Guna:*** *Laghu, Ruksha, Tikshna*
- ***Virya:*** *Ushna*
- ***Vipaka:*** *Katu*
- ***Doshakarma:*** *Kapha vatahara*
- ***Karma:*** *Kriminasana,*
- ***Rogaghnata:*** *Grahaka, Meha, Kushta, Arsha, Vrana, Vata, Adhmana, Kriminasanam param*
- *Beeja-Deepana, Pathya, Soola, Gulma, Vyathapaham, Kriminasanam param.*

***2. Shunti*[2]**

- ***Rasa:*** *Katu, madhura*
- ***Guna:*** *Guru, tikshna*
- ***Virya:*** *Ushna*
- ***Vipaka:*** *Madhura*
- ***Doshakarma:*** *Vatakaphapaha*
- ***Karma:*** *Deepana, Ruchya, Swaryam, Rochanam, Vrishyam, Hridyam, Bhedanam*
- ***Rogaghnata:*** *Gulma, Udara, Arsa*

*Kushta, Pandu, Raktapitta, Vrana, Vibandhaharam, Swayadhu, Prameha, Swasa, Kasa Prathisyaya, Alasaka, Avipaka, Kamala, Sosha, Manovikara.*

**3. *Sigru*[3]**

***Rasa:*** *Katu, Madhura*

- ***Guna:*** *Tikshna,Laghu*
- ***Virya:****Ushna*
- ***Vipaka:*** *Katu*
- ***Doshakarma:*** *Kapha vataghna (Pitta rakta prakopana)*
- ***Karma:*** *Deepana, Rochana, Vidahakrith, Chakshushya*
- ***Rogaghnata:*** *Vidradhi, Swayadhu, Krimi, Apachi, Visha, Pleeha, Gulma, Ganda, Vrana, Sopha, Amahara, Medoghna.*

**4. *Rasna*[4]**

- ***Rasa:*** *Tikta*
- ***Guna:*** *Guru*
- ***Virya:*** *Usna*
- ***Vipaka:*** *Katu*
- ***Doshakarma:*** *Vata Kapha hara*
- ***Karma:*** *Sophahara, Swasahara, Vatasulahara, Kasahara, Jwarahara, Visahara, Sidhmahara, Pachaka.*
- ***Rogaghnata:*** *Vatavyadhi, Sopha, Swasa, Kasa, Sula, Jwara, Sidhma, Agnimandhya, Visavikara, Amavata.*

**5. *Ugragandha*[5]**

***Rasa:*** *Katu, Tikta*

- ***Guna:****Laghu, Tikshna*
- ***Virya:*** *Usna*
- ***Vipaka:*** *Katu*
- ***Doshakarma:*** *Kapha vata samaka*
- ***Karma:*** *Medhya, Lekhana, Vamaka, Deepana, Vibandhahara, Adhmanahara, Sulaghna, Mutravisodhaka, Jantughna, Kanthya, Pachana, Mugharogahara, Swaraprada, Unmadarogahara, Apasmarahara, Jwaraghna, Atisaraghna, Bhutagna.*
- ***Rogaghnata:*** *Unmada, Apasmara, Sthoulya, Murcha, Agnimandhya, Ajirna, Arsas, Krimi, Udarasula, Jwara, Adhmana, Vibandha, Mukharoga, Atisara and Mutradosa.*

**6. *Varuna*[6]**

***Rasa:*** *Kashaya, Tikta, Madhura*

- ***Guna:*** *Laghu, Ruksha.*
- ***Virya:*** *Usna*
- ***Vipaka:*** *Katu*
- ***Prabhava:*** *Asmaribhedaka*
- ***Doshakarma:*** *Kaphavatasamaka due to usna virya and kaphahara due to Usna virya, Katu vipaka, and Kashaya, Tikta rasa.*

- ***Karma:*** *Mutrala*
- ***Rogaghnata:*** *Asmari, Mutrakrichra, Basti sula, Jwara, Krimi, Agnimandhya.*

**7. *Lasuna*[7]**
***Rasa:*** *Katu, madhura*
- ***Guna:*** *Tikshna, guru, Snigdha, pichila.*
- ***Virya:*** *Ushna*
- ***Vipaka:*** *Katu*
- ***Doshakarma:*** *Kapha vatahara*
- ***Karma:*** *Sara, Hridya, Kesya, Vrishya, Rochana, Deepana, Bhagnasandhanakrith, Balya, Raktha pitta pradooshana, rasayana*
- ***Rogaghnata:*** *Kilasa, Kushta, gulma, arsha, meha, krimi, hidma, peenasa, swasa, kasa*

**8. *Krishna*[8]**
- ***Rasa:*** *Katu*
- ***Guna:*** *Snigdha, laghu*
- ***Virya:*** *Anushna*
- ***Vipaka:*** *Madhura*
- ***Doshakarma:*** *Vatakaphahara*
- ***Karma:*** *Deepana, Vrishya, Rasayani, Rechana*
- ***Rogaghnata:*** *Swasa, Kasa, Udara, Jwara, Kushta, Prameha, Gulma, Arsha, Pleeha, Soola,*

***Ardra pippali****- Kaphaprada (Snigdha, seetala, Madhura, guru)*
***Sushka pippali****-Pitta vardhana*

**9. *Chitraka*[9]**
***Rasa:*** *Katu*
- ***Guna:*** *Tikshna*
- ***Virya:*** *Usna*
- ***Vipaka:*** *Katu*
- ***Doshakarma:*** *Vatakapha samaka, vata hara due to Usna virya, Kaphahara because of Usna virya, Katu rasa, and Katu vipaka.*
- ***Karma:*** *Deepana, Pachana, Kushtaghna, Arsoghna, Sothahara, Krimighna, Kasahara, Grahi, Rochaka, Kandughna.*
- ***Rogaghnata:*** *Agnimandya, Ajirna, Grahani, Kushta, Sotha, Krimi, Kasa, Arsas, Pandu, Udara, Kandu.*

**10. *Eranda*[10]**
***Rasa:*** *Tikta, madhura*
- ***Guna:*** *Guru*
- ***Virya:*** *Ushna*
- ***Vipaka:*** *Madhura*
- ***Doshakarma:*** *Vata nasana, (tridosha samana - Kai.ni)*
- ***Karma:*** *Tridosa samaka Vatahara due to Usna virya, and madhura vipaka, Pittahara due to madhura vipaka, Kaphahara due to Usna virya.*
- ***Rogaghnata:*** *Udavarta, pleeha, swasa, kasa, vardhma, asma nasana, udara, anaha,gulma, vasthisoola, anthravridhi, sonithavikara,meha, jwara, amavata, soola, sopha, kati, vasthi* and *siroruja.*

**11. *Suradaru*[11]**
***Rasa:*** *Tikta, Katu, Kashaya*
- ***Guna:*** *Snigdha, Laghu*
- ***Virya:*** *Usna*
- ***Vipaka:*** *Katu*
- ***Doshakarma:*** *Vata kaphahara Vatahara due to Usna virya, Kaphahara due to Usna virya, Katu vipaka and Tikta katu Kashaya rasa.*
- ***Karma:*** *Vibandhahara, Adhmanahara, Sothahara, Tandrahara, Hikkanigrahana, Jwaraghna, Pramehahara, Kasaghna, Kandughna, Swasahara, Arsoghna, Vedana sthapana.*
- ***Rogaghnata:*** *Vatavikara, Vibandha, Adhmana, Sotha, Tandra, Hikka, Kasa, Swasa, Jwara.*

**12. *Ghana*[12]**
- ***Rasa:*** *Tikta, Kashaya, Katu*
- ***Guna:*** *Laghu, Ruksha*
- ***Virya:*** *Sita*
- ***Vipaka:*** *Katu*
- ***Doshakarma:*** *Pitta kapha samaka, Pitta samana due to Sita virya and Tikta, Kashaya rasa.Kapha samaka due to Katu vipaka and Tikta, Kashaya, Katu Rasa.*
- ***Karma:*** *Jwaraghna, Atisāraghna, Rocaka, Dāhaśāmaka, Trsnă-nigrahāṇa, Śramahara Kapha sāmaka.*
- ***Indications:*** *Atisāra, Jwara, Aruci, Dāha, Trsṇā, Krimi.*

**13. *Pathya*[13]**
***Rasa:*** *Pancharasa* except *lavana*
- ***Guna:*** *Laghu, ruksha*
- ***Virya:*** *Usna*
- ***Vipaka:*** *Madhura*
- ***Doshakarma:*** *Tridosha samana, Vatanulomana*
- ***Karma:*** *Lekhana, Medhya, chakshushya, hridya, indriya prasadanam*
- ***Indications:*** *Meha, kushta, varna, chardi, sopha, vatarakta, mutrakrichra, Santarpanotha roganasana, Trishna, mukha sosha, hanusthambha, galagraha, navajwara, ksheena.*

**14. *Berbara*[14]**
***Rasa:*** *Katu, Tikta*
- ***Guna:*** *Laghu, Ruksha.*
- ***Virya:****Ushna*
- ***Vipaka:*** *Katu*
- ***Doshakarma:*** *Kapha-Vata hara, increases Pitta.*
- ***Karma:*** *Deepana, Krimighna, Jwaraghna, Shothahara, Kasahara, Shwasahara.*
- ***Indications:*** *Kasa (cough), Shwasa (asthma), Pratishyaya (rhinitis), Jwara (fever), Shotha (inflammation), Gulma, Hikka,* respiratory disorders.

**Table II: Integrated Ayurvedic Pharmacodynamics.**

| TERM | | PHARMACODYNAMIC EFFECT |
|---|---|---|
| ***Rasa*** | *Katu* (pungent), *Tikta* (bitter), *Kashaya* (astringent)<br>Minor: *Madhura* (in *Pathya*), *Lavana* (trace) | *Katu -Deepana, Srotoshodhana, Vata-Kapha shamana.*<br>*Tikta - Ama pachana, Lekhana,* anti-inflammatory<br>*Kashaya - Stambhana, Shoshana*, tissue stabilisation |
| ***Guna*** | *Laghu* -Enhances digestion & cellular uptake<br>*Ruksha* -Reduces *Kapha, Meda*<br>*Tikshna* -Rapid action, clears obstruction<br>*Sukshma* -Reaches microchannels (nerves, synapses)<br>*Sara* -Promotes movement of *doshas* | Breaks *Avarana* (obstruction)<br>Improves drug delivery to deeper tissues (*Majja, Snayu*)<br>Facilitates the quick onset of action |
| ***Virya*** | *Ushna Virya* predominantly | Stimulates *Agni* (metabolism)<br>Liquefies *Kapha* - removes stiffness<br>Pacifies *Vata* (especially *Avarana* type)<br>Improves circulation & nerve conduction |
| ***Vipaka*** | Mostly: *Katu*, *Vipaka* | Long-term *Kapha* reduction<br>*Lekhana* (scraping of *Ama* & *Meda*)<br>Maintains metabolic activation |
| ***Prabhava* (Specific Action)** | *Vata-Kapha hara* (especially neuromuscular disorders) | *Vedana sthapana* (analgesic)<br>*Shothahara* (anti-inflammatory)<br>*Srotoshodhaka* (channel cleansing, anti-oxidant)<br>*Akshepaka* & *Ardita shamaka* (antispasmodic + nerve stabilizing) |

In general, the formulation has action on:

- ***Vata:*** Normalises *Prana* & *Vyana Vata*, improves nerve conduction
  Relieves *Avarana Vata*, which is key in *Ardita* & *Akshepaka*.
- ***Pitta:*** Supports *Pachaka Pitta* (*Agni*)
  Prevents *Ama* formation
- ***Kapha*:** Reduces *Tarpaka* & *Shleshaka Kapha.*
  Removes heaviness in nerves & joints.

## PREVIOUSLY PUBLISHED: CORE THERAPEUTIC INDICATIONS AND CLINICAL APPLICATIONS

In contemporary clinical practice, *Dhanadanayanadi Kashayam* is frequently integrated into multimodal protocols to address progressive, degenerative, or acute neurological conditions in which *Vata* and *Kapha* are heavily vitiated.[15,16]

### 1. Facial and Cranial Nerve Palsies

The decoction is a standard clinical choice for managing Bell's Palsy (*Ardita*), where cold exposure or systemic imbalance causes sudden unilateral facial weakness.[15] Its *Vata-Kapha Shamana* qualities help resolve *Avarana* (the blocking of *Vata's* normal pathways by heavy *Kapha* attributes).[15,16] Case studies also validate its efficacy in secondary cranial neuropathies, such as Abducens (Sixth) Nerve Palsy, helping restore lateral ocular alignment and relieving diplopia (double vision) by rejuvenating localised nerve and muscle functions.[17]

### 2. Motor and Gait Movement Disorders

Clinical research highlights its integration into lines of treatment tackling focal dystonias like Blepharospasm—a condition characterised by repetitive, involuntary extraocular muscle contractions and forced eyelid closure.[18] Combining oral *Dhanadanayanadi Kashayam* with localised ocular therapies (*Netra Seka* and *Tarpana*) reduces facial muscular spasms and significantly boosts patient quality of life.[17] Furthermore, it is deployed in systemic nerve root compressions like Sciatica (*Gridhrasi*) to alleviate radiating lower back pain and associated leg numbness.[19]

### 3. Degenerative and Complex Ataxias

In complex, deep-seated neurodegenerative diseases such as Spinocerebellar Ataxia (SCA-2) and Progressive Bulbar Palsy (an aggressive motor neuron disease phenotype), *Dhanadanayanadi Kashayam* serves as a foundational internal medication.[20] When combined with specialised physical regimens (like specific yoga setups) and purification therapies (*Shodhana*), it directly works on *Majja Dhatu* (nervous tissue).[16,19] This comprehensive approach significantly lowers fall risks, stabilises postural sway indexes, and counteracts progressive neuromuscular weakness.

**Table III: Chemical Constituents, Class Of Compound And Their Actions.**

| Drug | Chemical constituents | Class of Compound | Actions |
|---|---|---|---|
| *Dhanada Nayana*[15] | Bonducin, caesalpinins, β-sitosterol | Terpenoids + Phytosterols (Steroidal compounds) | Immunomodulatory, antipyretic, anti-inflammatory, stimulates macrophage activity, improves glucose metabolism. |
| *Shunti*[21] | Gingerols, shogaols, zingerone, volatile oils | Phenolic compounds + Volatile (Essential) oils | Digestive stimulant, anti-inflammatory, antiemetic, carminative |
| *Sigru*[22] | Glucosinolates, isothiocyanates, quercetin, chlorogenic acid | Glucosinolates (organosulphur compounds) + Flavonoids + Phenolic acids | Anti-inflammatory, antioxidant, antimicrobial, digestive |
| *Rasna*[23] | Sesquiterpenes, flavonoids, sterols | Terpenoids + Flavonoids + Phytosterols | Anti-rheumatic, analgesic, anti-inflammatory |
| *Ugragandha*[24] | α-Asarone, β-Asarone, eugenol | Phenylpropanoids (volatile oil constituents) + Phenolics | CNS stimulant in low doses, improves cognition, enhances bioavailability, is carminative, and is a bronchodilator. |
| *Varuna*[25] | Lupeol, saponins, flavonoids, glucosinolates | Triterpenoids + Saponins (glycosides) + Flavonoids + Glucosinolates | Lithotriptic (anti-urolithic), diuretic, anti-inflammatory. |
| *Lasuna*[26] | Allicin, ajoene, sulphur compounds | Organosulphur compounds (volatile sulphur compounds) | Antimicrobial, hypolipidemic, cardioprotective, and digestive |
| *Krishna*[27] | Piperine, chavicine, volatile oils | Alkaloids + Volatile (essential) oils | Bioavailability enhancer, digestive stimulant, carminative |
| *Chitraka*[28] | Plumbagin, sitosterol, tannins | Naphthoquinones + Phytosterols + Tannins (polyphenols) | Strong digestive stimulant, anti-inflammatory, anthelmintic. |
| *Eranda*[29] | Ricinoleic acid, flavonoids, alkaloids | Fatty acids + Flavonoids + Alkaloids | Laxative, anti-inflammatory, Vata-pacifying |
| *Suradaru*[30] | Cedrol, himachalol, sesquiterpenes | Sesquiterpenes (Terpenoids / volatile oils) | Anti-inflammatory, analgesic, antimicrobial |
| *Ghana*[31] | Cyperene, cyperotundone, rotundone | Sesquiterpenes (Terpenoids / volatile oils) | Digestive regulator, antispasmodic, anti-inflammatory, antipyretic |
| *Pathya*[32] | Chebulagic acid, chebulinic acid, tannins, gallic acid | Hydrolysable tannins + Phenolic compounds (polyphenols) | Mild laxative, digestive, rejuvenative (Rasayana) |
| *Berbara*[33] | Serratagenic acid derivatives, β-sitosterol | Triterpenoids + Phytosterols | Bronchodilator, anti-inflammatory, anti-allergic, expectorant |

**Table IV: Phytochemical Classes And Bioactivities.**

| Functional Classification of Constituents | Actions |
|---|---|
| 1. Volatile Oils/Terpenoids[34,35]<br>Found in:<br>• *Vacha*<br>• *Shunthi*<br>• *Devadaru*<br>• *Musta*<br>• *Rasna* | • Increase digestive secretions<br>• Reduce intestinal gas<br>• Improve circulation<br>• Anti-inflammatory<br>• Mucolytic and bronchodilatory |
| 2. Phenolics and Flavonoids[36,37]<br>Found in:<br>• *Sigru*<br>• *Haritaki*<br>• *Bharangi*<br>• *Dhanadanayana*<br>• *Rasna* | • Antioxidant<br>• Protect vascular endothelium<br>• Reduce cytokine production<br>• Stabilise mast cells |
| 3. Alkaloids and Bioavailability Enhancers[38]<br>Found in:<br>• *Pippali* (piperine) | • Increase intestinal permeability<br>• Inhibit drug-metabolising enzymes |

| | |
|---|---|
| • *Vacha* (asarones) | • Enhance absorption of other phytochemicals |
| 4. Sulphur Compounds[39]<br>Found in:<br>• *Lasuna* | • Antimicrobial<br>• Vasodilatory<br>• Antiplatelet<br>• Cardioprotective |
| 5. Tannins[40]<br>Found in:<br>• *Haritaki* | • Gut mucosal protection<br>• Antioxidant<br>• Antimicrobial<br>• Modulation of microbiome |
| 6. Naphthoquinones[41]<br>Found in:<br>• *Chitraka* | • Stimulate digestive enzyme secretion<br>• Increase gastrointestinal blood flow<br>• Antimicrobial |

**Table V: Pharmacodynamics Of Constituents.**

| Sl no: | CLASS | CORE MECHANISM | MAIN OUTCOME |
|---|---|---|---|
| 1 | Terpenoids | NF-κB inhibition | **Anti-inflammatory Activity** |
| 2 | Flavonoids | Antioxidant enzymes increase | **Anti-aging Activity** |
| 3 | Phytosterols | Cholesterol competition | **Hypolipidemic** |
| 4 | Sulphur compounds | Detox enzyme induction | **Anticancer Activity** |
| 5 | Saponins | Membrane interaction | **Immunomodulation** |
| 6 | Alkaloids | Receptor binding | **CNS effects** |
| 7 | Quinones | ROS generation | **Antimicrobial Activity** |
| 8 | Fatty acids | Eicosanoid modulation | **Anti-inflammatory Activity** |

**Table VI: Adme Mapping.**

| Functional Classification of Constituents | ABSORPTION | DISTRIBUTION | METABOLISM | EXCRETION |
|---|---|---|---|---|
| **GROUP 1: LIPOPHILIC COMPOUNDS**[42]<br><br>**(Terpenoids, Phytosterols, Sesquiterpenes, Triterpenoids, Volatile oils, Phenylpropanoids)** | High lipid solubility, so passive diffusion.<br>Enhanced by bile acids<br>Rapid GI absorption | **Crosses cell membranes & BBB**<br>**Accumulates in fat, brain, and liver.** | Hepatic metabolism (CYP450)<br>Phase I oxidation | Bile (enterohepatic circulation)<br>Lungs (volatile oils) |
| **GROUP 2: POLYPHENOLS**[43]<br><br>**(Flavonoids, Phenolic acids, Tannins, Hydrolysable tannins, Naphthoquinones)** | Moderate to poor absorption<br>Often, as glycosides → need hydrolysis | Bound to plasma proteins<br>Limited CNS entry (except small phenolics) | Extensive Phase II conjugation<br>Glucuronidation, sulfation | Urine (major)<br>Some via bile |
| **GROUP 3: ORGANOSULPHUR COMPOUNDS**[44]<br><br>**(Glucosinolates, Volatile sulphur compounds)** | Converted to active forms (e.g., isothiocyanates)<br>Absorbed in the intestine | Widely distributed<br><br>**High affinity for detox tissues** | Conjugation with glutathione<br>Detox pathways | Urine (major)<br>Breath (volatile sulphur smell) |
| **GROUP 4: SAPONINS & GLYCOSIDES**[45]<br><br>**(Saponins, Triterpenoid glycosides)** | Poor absorption directly<br>Hydrolysed by gut flora | Limited systemic circulation | Gut microbial metabolism | Faeces (major) |
| **GROUP 5: ALKALOIDS**[46]<br><br>**(Alkaloids + volatile oils combinations)** | Good oral absorption<br>pH-dependent ionisation | **Widely distributed**<br>**Crosses BBB** | Hepatic metabolism | Renal (pH-dependent) |
| **GROUP 6: LIPIDS & FATTY ACIDS**[47] | Via lymphatics (chylomicrons) | Stored in adipose tissue | Beta-oxidation | $CO_2$ + water |

*BBB = BLOOD BRAIN BARRIER

**Table VII: Integrative Adme Mapping.**

| ADME | MECHANISM | EFFECT | BIO-MEDICAL TRANSLATION |
|---|---|---|---|
| **ABSORPTION**<br><br>*Shunti, Krishna, Chitraka* | *Katu* and *Tikta rasa, Laghu* and *Tikshna guna* | Stimulates *Jatharagni* & *Pachaka Pitta.* Enhances intestinal permeability<br><br>The *Yogavahi* effect of Piperine (*Krishna*) improves uptake, Rapid and efficient absorption | Gastrointestinal metabolic activation, modulation of tight junctions, and the micro-emulsification of phytoconstituents to enhance surface area absorption.[48,49]<br><br>Natural bioenhancement via temporary inhibition of hepatic cytochrome P450 enzymes (CYP3A4), suppression of intestinal P-glycoprotein (P-gp) mediated efflux, and alteration of epithelial cell membrane fluidity.[50,51] |
| **DISTRIBUTION *VYANA VATA*** | *Sukshma, Tikshna guna + Ushna virya* | Penetrates *Sukshma srotas* (microchannels)<br><br>Reaches *Majja dhatu* (nervous system)<br>Targeted delivery to neuromuscular sites | Passive transcellular diffusion of lipophilic small molecules across highly selective physiological barriers, including the blood-brain barrier (BBB) and systemic cellular lipid bilayers.[52,53] |
| **METABOLISM *(AGNI & DHATU PAKA)*** Drugs: *Chitraka, Shunti* | Enhances *Jatharagni + Dhatvagni* Performs *Ama pachana* | Proper biotransformation + toxin clearance | Phase I (oxidation/reduction) and Phase II (glucuronidation/sulfation) hepatic biotransformation, microbial-driven hydrolysis by gut microflora, and subsequent renal or faecal excretion.[54] |
| **EXCRETION**<br><br>Drugs: *Eranda, Varuna* | *Anulomana* (*Apana Vayu* regulation) Eliminates via *Purisha* & *Mutra* | Removes metabolic waste & clears channels | |

**PROBABLE MODE OF ACTION OF *DHANADANAYANADI KASHAYA***

Due to *Agnimandya*, *Ama* is formed, which, along with *Kapha*, causes *Srotorodha*, leading to *Avarana* of *Prana* and *Vyana Vayu*; this results in *Vata Prakopa* and *Majjavaha Srotas dushti*, manifesting as *Akshepaka* and *Apatanaka* as described in *Madhava Nidana*.

The formulation may exhibit a multi-target synergistic action beginning with *Deepana–Pachana* (**digestive-metabolic activation**) through agents like *Chitraka*, *Shunthi*, *Maricha*, *Vacha* and *Musta*, which enhance salivary, gastric and pancreatic secretions and improve intestinal motility, thereby correcting *Agnimandya* and preventing *Ama* formation. Simultaneously, **bioavailability enhancers** such as piperine (*Maricha*), asarones (*Vacha*), and gingerols (Shunthi) significantly increase the absorption and systemic availability of flavonoids, terpenoids, and other active constituents, thereby amplifying the overall therapeutic effect. The formulation further establishes a strong **anti-inflammatory** network, where *Rasna*, *Bharangi*, *Sigru*, *Devadaru*, *Lasuna*, *Musta* and *Varuna* inhibit key inflammatory mediators including COX, LOX, TNF-α, IL-1β and IL-6, thereby reducing chronic inflammation and **neuroinflammatory processes**.

In addition, respiratory-modulating actions of *Bharangi*, *Vacha*, *Shunthi*, *Lasuna* and *Devadaru* produce bronchodilation, reduce mucus viscosity and facilitate expectoration, contributing to *Kapha* clearance and ***Srotoshodhana***. The formulation also exerts gut–immune modulation, where *Haritaki*, *Musta*, *Dhanadanayana* and *Lasuna* improve microbial balance, reduce pathogenic load and enhance innate immunity with antioxidant protection, thereby reducing systemic inflammatory triggers.

At a deeper level, *Vata–Kapha* regulation is achieved through *Tikshna*, *Ushna* and *Sukshma* properties of *Vacha*, *Shunthi*, *Maricha*, *Chitraka*, *Devadaru* and *Rasna*, which liquefy *Kapha*, remove *Srotorodha* and restore normal movement of *Vata*. In modern pharmacological terms, this corresponds to anti-inflammatory (NF-κB inhibition), antioxidant enzyme activation, neurotransmitter modulation (via alkaloids), membrane stabilisation (phytosterols), detoxification (organosulfur compounds) and eicosanoid regulation (fatty acids).

Thus, the formulation interrupts the pathogenesis of *Akshepaka* and *Apatanaka* at multiple levels, correcting *Agnimandya*, eliminating *Ama*, clearing channel obstruction, stabilising neuronal excitability and protecting *Majja dhatu*, ultimately resulting in normalisation of *Prana* and *Vyana Vayu* functions and restoration of neuromuscular coordination.

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