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Review Article

An Updated Review on Recent In-Vitro, In-Vivo and Clinical Researches of Avipattikar Churna

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Abstract

Avipattikar Churna is used in clinical practice in dealing with the case of gastric disorders since the 19th century. Amla-pitta is one of the chief disorders of Gastro-intestinal tract. Colloquial term for Amla-pitta is Hyperacidity. Though various scientific researches were performed by varies Ayurvedic researchers, data of their outcome are not compiled to completely understand the pharmacology. This formulation promptly relives from major symptoms like Amlokalesh, Shirovedna, Ura-Pradesh Daha, Aruchi, Amlodgara. Neither, any complication(s)/Side effect(s) were reported so far, nor it produces addiction. 20 times of its normal dose (500mg/Kg body wt.) does not produce any acute toxicity in rats. Maximum numbers of constituents of it have Anti-ulcerogenic and Anti-oxidant property. It is an inference from all clinical study that 21- 45 days period is required to show marked improvement in the disease. Allopathic medicine uses to treat hyperacidity share a good portion of the drug market. Due to its higher safety and efficacy, it may be a good substitute for acid-lowering drugs of today.

Keywords: Amala-pitta, Rasapanchak, Gastritis, Biomarkers Anti-Ulcerogenic, Anti-secretory, Antioxidant, hyperacidity, Heart burn.

INTRODUCTION

Globally, the rate of deaths from non-communicable causes, such as heart disease, stroke, and injuries, is growing. At the same time, the number of deaths from infectious diseases, such as malaria, tuberculosis, and vaccine-preventable diseases, is decreasing [1]. In 2018, so have the lives of 41 million people claimed this year by non-communicable diseases. Though NCDs result in more than 2.5 times as many deaths as other causes, they commonly draw less notice than dramatic infectious disease outbreaks [2]. As social and economic conditions in developing countries change and their health systems and medical services improve. Contemporary medicines are easily available. Incidence of undergoing a prescription to over-the-counter switch also known as "Rx-to-OTC switch" is increasing [3]. The drugs are being pushed irrationally and the gullible doctors who depend on drug companies for their continued education believe their advice a hundred per cent. The pharma lobby even gets research data manipulated [4]. Topmost selling drugs are analgesic, antibiotics and gastric acid-lowering drugs. These drugs have too many prove side effects from minute to life-threatening [5, 6]. This rapid upsurge of technology in every field is responsible for continuously changing the human lifestyle. The increase in workload and short duration of achieving the target for the human being is suffering from physical & mental stress every minute. Lifestyle, food habits have been drastically changed. The craze for fast foods, which is a deficit of nutrients, irregular meals, work in shift duties, irregular sleep, long-distance travelling etc., imposes health negligence. Today is the age of cell phones, computer, and social networking websites or apps etc. All of these factors lead to various non-communicable diseases. The other cause of a sudden increase in NCDs is diet, smoking, stress, 1iver diseases, and genetic factors [7].

But due to the drawbacks of the allopathic medicines (mostly the safety issue) and other reasons, people are interested in herbal formulations [8]. For herbal medicines with a well-documented history of traditional use, need to qualify on safety and efficacy. So in 1991, WHO has developed and issued a series of technical guidelines such as "Guidelines for the assessment of herbal medicines", "Research guidelines for evaluating the safety and efficacy of herbal

medicines" and "Guidelines for clinical research on acupuncture" [9]. So in this direction so many Institute and Universities are conducted pharmacological pre-clinical and clinical researches in the Ayurveda under the guidance of CCRAS, CDSCO and ICMR. But the data of these are not accumulated. So, different important information is present here and there. Here we are compiling and summarizing the outcomes of the result of a very popular formulation used in the treatment of gastritis i.e., Avipattikar Churna. About one-third of the population is suffering from hyperacidity due to gastritis, NSAID induced and peptic ulcer disease and taking medicine for hyperacidity along with the treatment of other diseases like Hypertension, Analgesic, Blood thinner and others to suppress the gastric inflammation produced by them.

Amalapitta in Ayurveda

Agni (Digestive power) plays a powerful role in the physiological functioning of the body. Any alteration in the factor of Agni causes Roga (disease). Mandagni (diminish Digestive power) is the main root cause of all diseases [10] Mandagni leads to Ajeerna(Indigestion). Ajeerna if neglected gives rise to a vicious cycle called as Amla-pitta. Amla-pitta Vyadhi is a very common problem in socioeconomically developed as well as undeveloped countries. Though the intensity of this disease is not very high, its volume is very large. Pitta dosha has Kattu, amla Rasatmak, Tikshana, Ushana, Lahgu, Visra, Drava etc Guna (physiological property) [11]**.** When the Amla and Drava Guna of Pitta Dosha becomes exaggerated there is a sour blenching and this condition is regarded to be pathological condition termed as Amla-pitta. Types of Amla-pitta are: Urdhwaga, Adhoga, According to Dosha sansarga: Vatanubandhi, Kaphanubandhi, Vatkaphanubandhi [12, 13]. Kashyapa Samhita is the first available text which explained Amla-pitta as a separate entity [14].

Amla-pitta is mention since the Samhita period. Kulattha (*Dolichus biflorus*), Lavana Rasa, Viruddha Ahara etc. are described as the causative factors for Amla-pitta [15]. Sushruta Samhita describes the condition of Amlika similar to Amla-pitta because of excessive intake of Lavana Rasa[16].

Amalapitta vis-à-vis Hyperacidity

It is very difficult to correlate any disease mention in Allopathatic system with Vyadhi (disease) mention in Ayurveda. But based on of signs, symptoms and line of treatment mention in Ayurveda and modern medical science can be able to establish their similarity. So, in the same way, Amla-pitta cannot be correlated with one Acid Reflux syndrome which comprises with GERD, Gastritis, dyspepsia, peptic ulcer, hyperacidity [17]. The burning sensation in upper abdomen/chest, acid eructation, water brash, nausea, vomiting, vertigo and flatulence characterize it [18]. The Terms Dyspepsia and indigestion are difficult to define. Patients use these terms variously to express a feeling of epigastric fullness, discomfort or pain, heartburn, or acidity, nausea, vomiting, belching or flatulence [19]. Indigestion is a nonspecific term that encompasses a variety of upper abdominal complaints including nausea, vomiting, heartburn, regurgitation and dyspepsia (upper abdominal discomfort or pain). Some individuals with dyspepsia report ulcer-like symptoms such as epigastric burning or gnawing discomfort. Others experience symptoms of gastric dysmotility such as postprandial fullness, bloating, eructation (belching), anorexia (loss of appetite) and early satiety (an inability to complete a meal due to premature fullness) [20].

Avipattikar churna in Amalpitta

It is a fine powder of 14 different herbs, sugar and salt in a specific ratio. Complete formulation with different names is shown in table no.1. Indian Jalap is the chief ingredient, Second chief ingredient is clove. Candy sugar is added to mask the pungent and bitter taste of other content used in the formulation. Madhur Rasa (Sweet Taste) has Pitta-samak Property (Pitta Dosha suppressing property). People with a predominantly Pitta constitution is thought to be susceptible to hypertension, heart disease, infectious diseases, and digestive conditions [21].

Dose and Anupana: 10 gm daily in divided doses. Honey, water and Milk are used to potentiate the action of drug.

Table-1: Different names of ingredients and their composition

	Name of contents				
S.No	**Sanskrit**	**English**	**Hindi**	**Botanical Name**	**Ratio**
1	Shunthi	Ginger	Sonttah	*Zingiber officinale*	1
2	Maricha	Black pepper	Kali Marich	*Piper nigrum*	1
3	Pippali	Indian long pepper	Pippal	*Piper longum*	1
4	Amalaki	Indian gooseberry	Awala	*Embelica officinalis*	1
5	Vibhitaki	Belliric Myrobalan	Behada	*Terminalia bellirica*	1
6	Haritaki	chebulic myrobalan	Harad	*Terminalia chebula*	1
7	Vida lavana	Ammonium chloride	Vida namak	Ammonium Salt	1
8	Vidang	False black pepper	Vaividang	*Embelia ribes*	1
9	Nagarmotha	Nut grass	Musta	*Cyperus rotundus*	1
10	Ela	Cardamom	Choti Elaichi	*Elettaria cardamomum*	1
11	Tejapatara	Indian bay leaf	Tejpata	*Cinnamomum tamala*	1
12	Launga	Clove	Laung	*Syzygium aromaticum*	11
13	Nishotha	India Jalap	Trivrit	*Operculina turpethum*	44

14	Sarkara	Candy sugar	Mishri	Saccharum officinarum	66

Probable mode of action on the basis of Rasa Panchak

Most of the ingredient of Avipattikar churna having Katu, Tikta, Madhura Rasa, Laghu, Ruksha, Snigdha, Tikshna Guna, Ushna Sheet Virya, Madhura and Katu Vipaka. The main ingredient of Avipattikar Churna is Nishotha. It has Katu Rasa, Laghu, Ruksha, Tikshna Guna, Ushna Virya and Katu Vipaka. It has Bhedana and Rechana properties by Prabhav, so it leading to Pitta Virechana so useful in Samprapti bhang of Amlapitta. It has also contained Triphala which is mild purgative. All the drug of Avipattikar Churna having Deepana-pachana property which improves Agni and prevents Ama formation. Katu Rasa, Ushna Virya, Laghu, Ruksha, Tikshna Guna and Katu Vipaka help alleviation of Kapha. Once Kapha is alleviated Avarana of Vata gets removed and Vata transverse through its path leading to relief pain. Avipattikar Churna contains 66 part of sharkara, which has Pitta shamaka properties and Sheet Virya causes Shamana of Pitta and Daha. Rasadi Guna[22] of all contents is mention in table no 2.

Table-2: Raspanchak of Ingredients of Avipattikar churna

Latin name	Rasa	Guna	Veerya	Vipaka	Dosha karma
Zingiber officinate Roxb	Katu	Laghu Snigdha	Ushna	Madhura	Kapha vata shamak
Piper nigram Linn	Katu	Laghu , Teekhsna	Ushna	Katu	Kapha shamak
Piperlongum Linn	Katu	Laghu Snigdha Teekhsna	Anushna sheeta	Madhura	Kapha vata shamak
Emblika officialis Gaerth	Pancha rasa (Except Lavana)	Guru rukhsha sheeta	Sheeeta	Madhura	Tridosha samak
Terminalia chebula Retz	Pancha Rasa(Except Lavana)	Laghu rukhsha	Ushna	Madhura	Tridosha samak
Termininalia bellirica Roxb	Kashaya	Laghu rukhsha	Ushna	Madhura	Tridosha samak
Cyprus rotundus Linn	Katu tikta Kasaya	Laghu rukhsha	Sheeta	Katu	Kapha pitta shamak
Embelical ribes Burmf	Katu	Laghu ruksha teekhsna	Ushna	Katu	Kapha vata shamak
Elettaria cardamom Maton	Katu madhura	Laghu rukhsha	Sheeta	Madhura	Tridosha samak
Cinnamonam tamala Nees&Eberm	Katu tikta Madhura	Laghu ruksha teekhsna	Ushna	Katu	Kapha Vata shamak
Operculna trpethum Linn	Katu tikta	Laghu ruksha teekhsna	Ushna	Katu	Kapha pitta sodhak
Syzgium aromaticum Linn	Katu tikta	Laghu Tiksna	Sheeta	Katu	Kapha pitta shamak
Saccharum officinarum	Madhura	Sheeta snigdha	Sheeta	Ushna	Tridosha samak
Sanchal salt	Lavana	Laghu teekhna	Ushna	madhura	Vata shamak

Pharmaceutical Parameters: Aswatha Ram *et al*. do a comparative study on in-house preparation and formulation of two leading Ayurvedic pharmaceutical company such as Dabur and Baidyanath. Most of the parameters are within narrow difference but very few parameters show extreme limits.

Organoleptic analysis: Organoleptic study reveals that powder is light brown, sweet; odour is very pungent, characteristic to clove oil and fine in consistency [23]. Physico-chemical Analysis: [24, 25] Different values of Physico-chemical parameters are mentioned in table no 3.

Table-3: Physcio-chemical Characterization of formulation

Physcio-chemical Parameter	Values
pH (1%w/v)	4.853 – 5.090
pH (10%w/v)	4.556 – 4.983
Total Ash	2.952 – 3.57
Acid Insoluble Ash	0.356 – 1.197
Water soluble Extractive	53.81 – 58.246
Alcohol Soluble Extractive	15.97 – 19.59

Physico-chemical value of ingredients can be a good diagnostic to find out the adulteration is there or not. Individual values of different parameters are as shown in table no 4

Table-4: Physcio-chemical Characterization of contents of Formulation (n=3)

Name of Ingedient	Total Ash	Acid Insoluble Ash	Alcohol Soluble Ash	Water Soluble Ash
Piper nigrum	4.696±0.602	0.330±0.074	20.136±0.304	11.502±0.255
Piper longum	4.842±0.396	0.473±0.075	14.226±0.518	14.931±0.433
Terminalia chebula	2.778±0.414	0.115±0.028	98.714±0.648	98.230±0.340
Terminala bellirica	4.218±0.452	0.294±0.093	69.726±1.395	39.604±0.304
Embelica officinalis	4.178±0.637	0.381±0.3290	51.630±0.417	77.256±0.329
Emblia ribes	4.738±0.702	0.194±0.052	15.972±0.406	10.418±0.700
Elletaria cardamomum	2.626±0.232	2.991±0.201	20.846±0.256	11.549±0.549
Cyprus rotundum	3.643±0.217	3.595±0.136	17.395±0.406	26.221±0.376
Cinnamomum tamala	3.505±0.271	0.210±0.179	26.0±0.518	20.534±0.461
Syzyium aromaticum	3.624±0.658	0.635±0.089	31.574±0.527	41.485±0.546
Saccharum offinrum	0.199±0.099	0.398±0.050	28.359±0.497	167.883±0.589
Zingiber offinale	5.689±0.072	0.643±0.025	7.871±0.577	24.47±0.331
Operculina terpethum	4.147±0.101	0.394±0.184	17.209±0.314	13.972±0.364

Physical characteristics of powder formulation

Powder flow is the displacement of powder particles concerning each other, under the effect of some directional force (gravity, entrainment in a fluid stream, the mechanical force of an auger, scraper, vibrator, agitator, mixer, etc., and, occasionally, electrostatic forces)[26]. So it is useful parameters related to powder flowability [27, 28].

The tapped density is an increased bulk density attained after mechanically tapping a container containing the powder sample. Bulk density refers to the method used to indicate a packing of particles or granules. The angle of repose has been used as an indirect method quantifying powder flowability, because of its relationship with interparticle cohesion. Hausner ratio is related to interparticle friction and as such can be used to predict the powder flow properties. The Carr index (also: Carr's index or Carr's Compressibility Index) is an indication of the compressibility of a powder.

Table-5: Evaluation of flow ability of powder

characteristic	Value	
Tap density	0.477 – 0.555	
Bulk Density	0.417 – 0.487	
Angle of repose	38.46 – 41.05	Passable
Haussner ratio	1.129 – 1.143	Good flow characteristic
Carr's Index	11.43 – 12.53	Excellent relative flow ability

The powders completely pass on through sieve number 44 and not less than 50 per cent pass on through sieve number 85.

Sodium content was estimated by using a flame photometer 7.2 - 12.7 %. Phytochemical of Avipattikar churna: Churna shows the presence of various phytoconstituents like tannins, flavonoids, saponins, sterols, alkaloids, and glycosides, anthraquinone, carbohydrates etc [29].

Element determination

Energy dispersive x-ray spectroscopy (EDX) is a technique used for the elemental analysis and chemical characterization of a sample. Different sample types (solid materials, liquids, powders, metals, minerals, etc.) can be analyzed with simple sample preparation over a wide range of concentrations (from traces to main components) is possible without dilution [30].

Flame Photometry, a branch of atomic spectroscopy is used for inorganic chemical analysis for determining the concentration of certain metal ions such as sodium, potassium, lithium, calcium, Cesium, etc.

Comparison of results obtained from flame photometry and EDX was done and illustrated in table no. 6

Table-6: Comparision of elemental determination

Element	Flame Photometery	EDAX
Na^{+}	0.2508 -0.325	0.50 – 0.58
K^{+}	0.325 – 0.4736	0.46 – 0.60
Ca^{2+}		0.55 – 1.42
Cu^{2+}		1.39 - 3.15
Zn^{+}		1.24 – 2.71
Cl^{-}		0.65 – 1.04

Acute toxicity study

Study of toxicity on 6 groups Swiss albino mice by Awatha Ram H N *et al*. They were fed with Aqueous solution of Avipattikar Churna suspended in

2% gum acacia, in different dose levels of 100, 500, 1000, 3000, 6000 and 10,000 mg/kg body weight. The mice were observed continuously for 2 hr [31] for behavioural, neurological and autonomic profiles and after a period of 24 and 72 hr for any lethality [32]. Acute toxicity was carried out and the extract was found to be safe up to a dose of 10,000 mg/kg [33].

Anti-Secretory and Anti-Ulcerogenic Activities on Peptic Ulcers: Gyawali S. *et al.* study was carried out to evaluate the relative anti-secretory and the anti-ulcerogenic activities of the Churna with that of ranitidine in a pyloric ligated model of Sprague Dawley male rats [34]. In this study, four groups of rats (with 6 animals in each) served as the ulcer controls, Churna low dose (500 mg/kg), Churna high dose (750mg/kg) and ranitidine (25mg/kg). The control group rats received only vehicle {2% (v/v) gum acacia}, while the rats of the other groups received the respective dose of the Churna or ranitidine which was suspended in the vehicle. The treatments were given twice a day, orally, for two days. After 1 hour of the last dose, pyloric ligations were performed and the rats were sacrificed for evaluation after four hours of the ligations. The gastric contents were collected and its volume, pH and acidity were measured. The numbers of ulcers and their lengths were measured which were used to calculate the gastric irritancy index and the curative ratio. The test drug, Avipattikar churna, showed anti-secretory and anti-ulcerogenic effects against the gastric ulcers which were induced by a pyloric ligation. The anti-secretory and the anti-ulcerogenic activities of the churna at a 500 mg/kg dose were similar to those of ranitidine. A good therapeutic effect was observed in the Churna.

Gastro protective action of Avipattikar churna by pretreatment model was done by Aswatha Ram *et al.* in Albino Wister rat dose of 500 mg/kg. In this study, three different models of ulcer induction are selected for study which is as Ibrupfen (300mg/kg), Ethanol (1ml/animal), and Pylorus ligation [33]. Each model consisted of 3 groups of 6 rats each. Every subgroup of each model is treated with 2% gum acacia (Vehicle) for control, Reference standard drug is Ranitidine at a dose of 25mg/Kg, and Aqueous solution of Avipattikar Churna in a dose of 500mg/kg. Gastric volume, free acidity, total acidity, ulcer number {UN}, gastric irritancy size {GIS} and gastric irritancy index {GII} were the parameters taken. GII is calculated by multiplication of UN with GIS. One way ANOVA followed by post hoc Sheff's test using is used for statistical analysis of the result. The effects of formulation were found to slightly lower with that of the standard drug in reducing the ulcer number and gastric irritancy index. In the present study administration of Avipattikar Churna at a dose of 500 mg/kg, exhibited marked gastroprotection.

Similar kind of study was conducted by Zaveri M & Patel V at the dose of 540 mg/Kg, standard reference drug was omeprazole and one way ANOVA test followed by Tukrey's multiple range tests. Ethanol-induced gastric mucosal damage model and pylorus ligation model was taken for study [29]. Every model is subjected to three types of the treatment group. Group I- received 1 % carboxy methylcellulose (Vehicle), Group II received an aqueous extract of Avipattikar Churna at a dose of 540 mg and Group III received standard drug omeprazole at a dose of 20 mg/ kg PO. In the first model ulcer index and lipid peroxidation were the parameters are taken. Ulcer index is calculated by the following equation. Ulcer index =10/X, where X= (Total mucosal area)/ (Total ulcerated area). In pylorus ligation model ulcer index, acid secretory parameter mucoprotective parameters. Acid Secretory parameter has a bundle of analytical test such as gastric acid volume, total acidity, pepsin activity pepsin output. Mucoprotective effect evaluation was assessed by two analytical parameters such as mucous content and mucous activity. Mucous activity is a ratio of total carbohydrate and protein content. This study reveals that Avipattikar Churn is 1.5 to twice time effective.

Antioxidant activity: The free radicals played an important role in lipid peroxidation in the development of ulcers is revealed by recent studies [35]. The free radicals produced cause lipid peroxidation, leading to membrane fluidity which in turn increases the influx of Ca^{2+} ions and results in the reduced membrane integrity of surface epithelial cells, thereby generating gastric ulcers [36, 37] Free radicals have been demonstrated as a contributing factor in tissue injury and the modulation of pain [38]. The incidence of ethanol-induced ulcers, predominant in the glandular part of the stomach has been reported to stimulate the formation of leukotriene C4 (LTC4), mast cell secretory products[39] and reactive oxygen species[40] resulting in the damage of rat gastric mucosa[41]. antioxidants like ascorbic acid (Vitamin C), α- tocopherol (vitamin E), glutathione (GSH), carotenoids, flavonoids, etc. act by one or more of the mechanisms like reducing activity, free radical scavenging, potential complexing of pro-oxidant metals and quenching of singlet oxygen [42] Antioxidants may offer resistance against the oxidative stress by scavenging free radicals, inhibiting lipid peroxidation and by many other mechanisms and thus prevent disease [43]. In vitro, antioxidant activity study of Avipattikar Churna in aqueous extract and methanolic extract show the highly significant result in comparison with ascorbic acid. The free radical scavenging activity was carried out using the reactivity of extracts towards different radicals such as 2,2 – Azino bis (3-ethyl Benzo Thiazole – 6 – Sulphonic acid (ABTS), 1,1-Diphenyl-2- Picryl Hydrazine (DPPH) and 1:10-Phenanthroline hydrate (O-phenanthroline).

The superoxide scavenging activity was measured by the spectrophotometric method using (Nitroblue tetrazolium) NBT. The total antioxidant

potential of aqueous and methanolic extracts of Avipattikar churna was also evaluated [44].

Clinical Study on Amla-pitta

A clinical interventional single-blind trails of Avippatikar churna was done by Sharmili Vijay Suryavanshi in 30 patients of Amla-pitta having the age of 20-70 years. Patients of PUD or gastric malignancy were excluded. The assessment criteria were based on symptomatic relief by assigning different grades between 0-3. The sign and symptom of disease were a quote from the compendium of Madav [45] and Yogratankar[46] Follow up of patients was done after every 7th days. Result of the study is depicted in table no 7.

Table-7: Percentage of symptomatic relief after the treatment with Avipattikar Churna

		Uppashya		Anupashya
S.No	**Sign and Symptoms**	**Complete Relief (%)**	**Partial Relief (%)**	**No Relief (%)**
1	Tiktaamla udgar	59.02	29.06	11.11
2	Hrudkantha daha	79.02	13.07	06.08
3	Aruchi	69.56	21.07	8.69
4	Utklesha	81.25	18.75	00
5	Udar shula	47.82	39.13	13.04
6	Udar gaurava	81.25	18.75	00
7	Adhamaan	65.00	19.02	15.03
8	Shir shula	62.96	18.05	18.05
9	Praseka	80.95	09.05	09.05
10	Hrullas	60.00	20.00	20
11	Chardi / Vaman	92.30	00	7.60
12	Madangani	84.00	16.0	00
13	Hastapadtal daha	44.00	11.11	44.44

Simple statistical tools such as percentage and also paired t-test have been used to tabulate the collected information. The P-value was 0.0003 which was extremely statistically significant, t =5.2675 and df =11. In his study, Avipattikar churna has shown good results on Tiktaamlaudgar, Hrudkantha Daha, Aruchi, Utklesh. The largest number of patients belonged to the age group of 20 - 40 yrs. It is also ruled out that Chinta (mental stress) also shows considerably largest contributory factor for disease aetiology.

Another interventional single-blind study was performed by Ravte R K *et at*. in 10 OPD patients of NIA Jaipur, India. Patients have been known case of PUD and Gastric malignancy was also excluded. The trial was conducted for 21 days with 7 days interval follow up. Some important finding related to etiological factor and assessment of the composition of the body on Ayurvedic Parameters are shown in table no.08.

Table-08: Etiology and composition of body's parameter

Findings of study		**Percentage**
Maximum no of patients belongs to age group of 31- 40		50
Service Class Occupational category (mental Stress)		50
Patients were having Madhya kostha, (moderate digestive strength)		50
Shareera prakrit (Body Composition)	Vata-Kapha (Maximum)	40
	Vata-Pitta (Next to maximum)	30
Addition	Tea & Coffee	90
	Alcohol	10
	Smoking	20
	Tobacco	10
Response to Treatment in patients	Significant relief	70
	Moderate relief	30
Major Symptomatic relief	Amlotkalesh	66.66
	Shirovedna	53.33
	Ura-pradesh Daha	64.00
	Aruchi	60
	Amlodgara	75

Clinical evaluation of Effect of Avipattikar Churna was assessing on gastric specific biomarkers (Shown in table no 09) of Amla-pitta by Mahanja M P & Hendre S M also confirms its potential for Gastric disorders. Every cell type has a unique molecular signature, referred to as biomarkers, which are

identifiable characteristics such as levels or activities (the abilities of genes or protein to perform their functions) of a myriad of genes, proteins or other molecular features. Therefore Biomarker is an objective measure or evaluation of the normal biological process, pathogenic processes or pharmacological responses to a therapeutic intervention [47]. In this study, 10 patients were selected for 30 days of observation and review was done at an interval of 7 days. Patients were treated with 8 gm of Avipattikar Churna in 2 divided doses. Half of the patients received treatment get 80% relief [48].

Table-09: Gastric specific Biomarker

Bio Marker	Abbreviation	Diagnostic application
Pepsinogen – 1	PG - 1	Gastric Acid Secretion
Pepsinogen – 1	PG - 2	Gastric Inflammation Marker
Gastrin – 17	G - 17	Reflux Disease
IgG For H. Pylori	IgG HP	Antibodies against H. Pylori

Comparative clinical study with other formulation

A clinical efficacy trial is often required to further demonstrate comparative safety and effectiveness of the two products [49, 50]. An open comparative interventional study is conductive on 2 groups having 30 patients in each group. Only cardinal features Aruchi, Tikta Amlodgara, Utklesh, Hrud Kanthadaha and Klama were chosen for the study to show relative efficacy between it and Patoladi Kwatha [51]. In Table 10 summary of the study is presented.

Table-10: Detail of formulations and their result

Grouping and posology		
	Group A	**Group B**
Name of Formulation	Avipattikar Churna	Patoladi Kwath
Reference	Bhaishajaya Ratnavali 56/24-28	Chakradatta 52/19
Route of Administration	Oral	Oral
Time of Administration	Twice a day after meals	Twice a day after meals
Anupana	Sheetal Jala	
Duration of Therapy	45 days	45 days
Result of the treatment		
(a) Effective Cured	43.33 %	23.33 %
(b) Moderate Improvement	33.33 %	36.66 %
(c) Mild Improvement	10 %	10 %
(d) In significant	13.33 %	30 %

The overall effect of the Avipattikar churna with proper diet and regimen was more significant and better than the effect of the Patoladi kwath after treatment and even follow-up. No any side effects or adverse effects were observed during the study [52].

Additive effect Study with Avipattikar Churna

When two or more drugs are given simultaneously or in quick succession, they may be either different to each other or exhibit synergism or antagonism. When the action of one drug is facilitated or increased by the other, they are said to be synergistic [53]. Sutashekhar Rasa, Kamadudha Rasa, Shankha Bhasma, Prawal Panchamrita Rasa, Kapardhika Bhasma, Mandura Bhasma, Yastimadhu Churana, Vachadi Churna, and Dhatri Lauha etc are used to amplify the action of Avipattikar Churna in combination[54, 55].

A clinical trial was conducted on 33 patients to assess the additive effect of two formulations for hyperacidity. All the subjects were treated with Avipattikar Churna 1gm along with Kapardika Bhasma 500 mg twice in a day orally with normal water after food for 30 days.

All the subjects were followed up on every 10th day for a period of 30 days. In this study, the average age of patients was 35 years and the ratio of male and female 6:4. The assessment was done only on subjective parameters Amlotklesha (Acid Eruction), Praseka (Water brash), Chhardi (Vomiting), Utklesha (Nausea), Bhrama, (vertigo), Adhamana (Flatulence), Vibandha (constipation) and tenderness in the upper abdomen, by assigning different grades. Percentage of relief was calculated on the basis of this formula = Total score of before treatment (BT) - Total score of after treatment X 100/ Total score of before treatment (BT). A good number of patients responded to the treatment. None of the patients shows no response to the treatment [56].

Another open single-arm clinical trial was conducted on 113 patients to assess the additive effect of two formulations for hyperacidity. The dose of trial drugs taken for the study was a combination of Avipattikar Churna 5 mg and Sutasekhar Rasa 125 mg

twice a day 30. Patients having Hypertension, Diabetes Mellitus II, Renal failure, Liver disorders, COPD and Asthma were excluded. Routine pathological laboratory tests, Hematological investigations, Urine and stool examination were performed to rule out any wrongful of the trail. Only Cardinal Features were selected for the study. These were Avipaak (Indigestion), Klama (Tiredness), Utklesaa (Nausea), Tikta-Amala Udagar (Sour and pitta belching), Gauratava (Heaviness), Hrit-Kantha Daha (Heart and throat burn) and Aruchi (Anorexia). A grade between 0-4 is allotted to the patients after careful observation of symptom. Wilcoxon sum rank test is used for statistical examination of result data. Some important observation of the study are summarized in Table 11

Table-11: Summary of observation of trail

Observed Features	Category of Maximum	%	Category of Minimum	%
Gender	Male	85	Female	24.78
Age-wise prevalence	30 – 35 years	24.78	66 – 70 years	0.88
Occupation	field workers	27.48	Business	3.54
Nidan	Ati-lavan-Amla-Tikshan ahaar Seven	57.52	Vega vidharana	33.52
Clinical Fearture	Hrita-kantha Daaha	100	Klama	44.25

This combination also shows significant improvement in 4 weeks of administration of drugs in all assessment parameters of Amla-pitta. Follow up were done in four weekly sittings [57].

DISCUSSION

Standardisation is an essential factor for the polyherbal formulation to assess the quality of drugs based on the concentration of their active principle. It is very important to establish a system of standardisation for every plant medicine in the market since the scope of variation in different batches of medicine is enormous. Plant material, when used in bulk quantity, may vary in its chemical content and therefore, in its therapeutic effect according to different batches of collection e.g. collection in different season and/or collection from sites with the different environmental surrounding or geographical location. The increasing demand of the population and chronic shortage of authentic raw materials have made it incumbent, so there should be some sort of uniformity in the manufacture of Ayurvedic medicines to ensure quality control and quality assurance [58]. Various pharmacognostic aspects of Avipattikar Churna were studied by different researchers. But TLC and HPTLC fingerprinting profile studies and Microscopic study was an untouched area. Aforementioned analytical test exhibits a set of diagnostic characters, which may help in identifying the drug in dried condition. It is necessary to develop methods using phytochemical markers uniformity of batches in production of Ayurvedic formulations [59]. Moderate pH value and high water-soluble extractive value is suggested that it starts working from the stomach.

Avipattikar Churna has perfect combination of 12 Spices and salt and sugar. They have many valuable phytochemicals and elements. Some important biological role of ingredients of Avipattikar Churna is necessary to understand the probable mode of action. Vida Lavana contains a small amount of trace elements such as iron and magnesium. It is carminative and tonic to the digestive system. It replenishes salt lost in exercise and adding to trace elements essential for normal health and fitness. Potassium, sodium, chloride helps in regulation of Na/K/Ca ATPase, glucose transport, transport of some amino acids including alanine, proline, tryptophan and tyrosine. Potassium ions are involved in several of essential physiological processes, such as the maintenance of intracellular acid-base balance and tonicity. Copper aid enzymes, specifically in the oxidation of iron. Zinc is essential in reactions involving syntheses such as carbohydrates, lipids, proteins and nucleic acids [60]. In a study, five phenolic amides Maricha (*Piper nigrum*) found to possess significant occurring antioxidant, α-tocopherol [61]. Hydroalcoholic and Methanolic extract of stem bark of Trivrit (*Operculine terpenthum* Linn) possess enhanced ulcer preventive and protective activities when compared with standard drug ranitidine. Extracts of *Operculine turpenthum* were administered in a dose of 100 mg/ Kg body weight orally and effects were evaluated employing aspirin ligation model in experimental rats [62]. Phytochemical analysis of Amala (*Emblica officinale*) was found to be the inhibitoriest towards all the pathogens. These Phytochemical acts as Antimicrobial, anti-ulcerous, etc [63]. The extract obtained from the fruits of Vebhitaka (*Terminalia bellercia*) has laxative, anti-microbial, antioxidant, analgesic, anti-ulcerogenic effect *et al*. [64]. Zerumbone, a sesquiterpene and gingerol, a plant phenol both active constituents of another ingredient of Avipattikar churna, *Zingiber officinale* are reported antioxidants. It was also reported the ability of aqueous extract of *Piper longum*, *Zingiber officinalis* to augment mucin secretion and to decrease cell shedding in the stomach of the rat [65].

Studies on relative efficacy on Avipattikar Churna are very less. Even almost clinical studies were done on a very small sample size. Management of Amla-pitta by Avipattikar churna of Ayurvedic system of medicine is still superior to that of another system of medicine because there is no case of side effect is seen

in any clinical studies. The fragrance of clove works as a mouth freshener and sweet taste made it readily acceptable.

Amla-pitta is mostly a psychosomatic disease and the incidence of the disease will be increased in parallel with the advanced of civilization and condition of the society. Patients having Vatapitta Prakriti are more affected by this disease than other Prakriti. Patients of Middle age group are more affected by this disease than other age groups. This age of life span has an upsurge of pitta that is mentioned in every classic of Ayurveda [66]. Married persons are more affected by this disease than unmarried. Patients having mental stress are more affected by this disease. Not any side effects or adverse effects were observed during the study. Variation in the age group is seen in different studies because of the election of different ages in groups and the size of the sample for the study.

CONCLUSION

Avipattikar Churna is the oldest drug for Gastric acid disorder. Avipattikar Churna is an effective remedy of hyperacidity in a dose of 6 to 10 gm. In-vivo studies not only confirm the effectiveness of the formulation but provide more evidence of the safety and efficacy of the formulation. Different Clinical research displays Avipattikar Churna possesses significant gastro-protective activity. Contents of the drugs are very effective in curing the hyperacidity of multiple etiologies. Sutsekhar Rasa, Kapardika Bhasma and other calcium and iron-containing formulation are capable to synergistically potentiate the effectiveness of the drug.

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