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Observational research on the effect of an Ayurvedic treatment protocol in patients of hereditary pancreatitis

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ABSTRACT

Background: Hereditary pancreatitis (HP) is a chronic and recurrent inflammatory disorder caused by genetic abnormalities, often accompanied by severe symptoms and complications. Conventional treatments offer limited relief but fail to halt disease progression. An Ayurvedic Treatment Protocol has been reported to be effective in treating various types of pancreatitis.

Objectives: This observational clinical study is aimed at assessing the efficacy of a year long Ayurvedic treatment protocol (ATP) in mitigating attack frequency and intensity in Hereditary Pancreatitis patients.

Materials & Methods: The study enrolled 151 patients across diverse age groups and genders, subjecting them to a comprehensive Ayurvedic treatment protocol at a specialized center. The protocol incorporated Metal-Based Ayurvedic Formulation (MBAF) named Amar, alongside supportive Ayurvedic compounds and dietary adjustments. Patients underwent pre- and post-treatment evaluations involving interviews, medical records, blood tests, radiological imaging, and symptom assessments. Notably, pancreatic enzyme use was discontinued prior to initiating Ayurvedic treatment.

Results: Among 151 patients, 88 completed the year long ATP, resulting in significant enhancement of their quality of life. There was a marked 98.7% reduction in emergency hospitalizations and a notable 92.8% decrease in attack frequency ($p < 0.0001$). Radiological assessments indicated pancreatic health stabilization, while no adverse effects were reported, highlighting the intervention's safety and tolerability.

Conclusion: The study furnishes promising evidence supporting the efficacy and safety of ATP, especially the MBAF, in managing Hereditary Pancreatitis. The observed decline in attack frequency, absence of adverse effects, and stabilization of pancreatic health underscore the potential of Ayurvedic medicine. Subsequent research, including randomized controlled trials, is warranted to substantiate these findings and elucidate underlying mechanisms.

1. Introduction

Hereditary Pancreatitis (HP) is defined as a rare gastroenterological disease characterized by genetic mutations for Pancreatitis or recurrent acute pancreatitis and/or chronic pancreatitis in at least 2 first-degree relatives, or 3 or more second-degree relatives in 2 or more generations, for which no predisposing factors are identified [1]. Despite sharing similar symptoms with acute, recurring, and chronic pancreatitis, HP is marked by the presence of specific mutated genes in the patient's serum. These mutations, known as "misfolding" mutations, disrupt the proper folding of digestive enzymes in the endoplasmic reticulum (ER) [2]. While HP can manifest in children, adolescents, and adults, it carries a higher morbidity rate compared to other forms of pancreatitis [3]. Molecular genetic testing techniques vary, ranging from single-gene tests to multi-gene panels, aiding in its diagnosis [4]. Importantly, the risk of pancreatic cancer is substantially elevated in individuals with hereditary pancreatitis, reaching up to 55% [5].

First identified by Comfort and Steinberg in 1952, HP was classified as a form of pancreatitis prone to recurrence and prevalent among blood-related groups based on Mendelian inheritance patterns [6,7]. Subsequent discoveries in the late 1990s pinpointed mutations in the PRSS1 gene as the root cause of most HP cases. When a PRSS1 mutation

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is inherited, the risk of developing HP is around 80%, with a near 40% lifetime chance of developing pancreatic cancer, rising to 75% if the mutation is inherited paternally [8].

Standard treatments for HP involve emergency hospitalization during acute episodes, encompassing intravenous fluids, pain relief medications, enzyme supplementation, antibiotics, and a life-long adherence to a diet low in fats and proteins [9]. However, due to the progressive nature of the disease, the increasing financial burden, and the limitations of conventional treatments, patients often explore alternative therapeutic approaches to alleviate symptoms. While conventional interventions manage the consequences and temporarily relieve pain, they fall short in halting disease progression [10].

Complementary and alternative medicine systems, including Ayurveda, Unani, Siddha, Homoeopathy, and Yoga, are considered independent medical approaches alongside conventional medicine [11]. Ayurveda, a traditional Indian system, places great emphasis on diet, lifestyle, and medicines derived from plant, animal, and mineral sources [12]. Among its specialized fields, *Rasa-Shastra*, translating to the "Science of Mercury," deals with the therapeutic application of processed metals and minerals. The safe use of these substances involves the process of sublimation with Sulphur to enhance their therapeutic properties [13].

Remarkably, a North Indian-based Ayurvedic Physician has reported significant and enduring benefits of *Ayurvedic* interventions in treating various forms of Pancreatitis, including Hereditary Pancreatitis. 1750 patients suffering from different variants of Pancreatitis were enrolled at the clinic for Ayurvedic treatment between January 1997 to July 2023. Of these, 151 patients were suffering from Hereditary Pancreatitis and the first patient of HP was enrolled in October 2001. This study delves into the substantial advantages of *Rasa-Shastra* in managing the complex challenges posed by Hereditary Pancreatitis.

2. Methodology

The Ayurvedic treatment for Pancreatitis started in January 1997 with the enrolment of the first patient. Earlier the diagnosis was confirmed on the basis of written ultrasound reports by the treating gastroenterologists. Later, with more studies stating the role of MRCP in the diagnosis of Pancreatitis, MRCP became the diagnostic method of choice from November 2014. Similarly, tests and supplements for Vitamin D3 and B12 were also introduced around the same time. Deworming was introduced as a part of the practice for every patient in 2013.

This paper discusses the effects of Ayurvedic treatment protocol in 151 patients of Hereditary Pancreatitis. These patients started treatment between October 2001 and July 2023. The treatment plan commenced with an initial three-week residential phase in Uttarakhand, India.

This study encompassed individuals spanning an age range of 3–62 years, comprising both males and females. Demographic and symptoms details are provided in Table 1. A thorough examination of the participants' medical history revealed 1351 distinct attacks and 873 emergency hospitalizations. Detailed interviews were conducted to collect comprehensive information on symptom onset, diagnostic procedures, hospitalizations, enzyme usage, and personal profiles, including dietary preferences, origin, education, occupation, and family history. All these details were meticulously documented during the history taking. Prior to the commencement of the Ayurvedic treatment, participants underwent a battery of baseline tests, including hemogram, lipid profile, liver and kidney function tests, diabetes profile, CRP, vitamin levels, serum amylase/lipase, and Carbohydrate Antigen 19-9 assessment, aimed at assessing their health status.

The diagnosis of hereditary pancreatitis (HP) was established based on a combination of family history and the identification of gene mutations. Modern diagnostic techniques, including ultrasound, Magnetic Resonance Imaging (MRI), Endoscopic Retrograde Cholangiopancreatography (ERCP), Computerized Tomography (CT) scans, and blood tests, were employed to discern variations in pancreatitis diagnosis. Some patients had undergone stenting and were already undergoing enzyme treatment. Prior to the initiation of Ayurvedic therapy, a thorough review of previous medical records was conducted, alongside new Magnetic Resonance Cholangiopancreatography (MRCP) procedures.

The treatment protocol included the administration of a Metal-Based Ayurvedic Formulation named Amar at a dosage of 4 mg per kg of body weight per day, divided into three doses to be taken during meals. This core treatment was complemented by supportive Ayurvedic formulations such as Prak-20, *Kamdudha Ras, Soothsekhar Ras, Narikel Lavana, Rason Vati, Chitrakadi Vati*, which were prescribed based on abdominal examinations and presenting symptoms (Table 2). All these formulations are prepared under the author's guidance and an authorized manufacturing license by his manufacturing unit. A personalized dietary plan was provided, distributed across three main meals and three snacks daily. Prohibited items included alcohol, caffeinated and carbonated beverages, pre-packaged and reheated foods, as well as foods containing onions, tomatoes, garlic, tamarind, and refined flour. Patients were advised to ensure a minimum of 8 h of nightly sleep and to practice both mental and physical rest.

Patients who did not undergo deworming in the last six months were administered an initial dose of 400 mg of Albendazole for two consecutive days [14]. Those with low vitamin D3 levels received a weekly dose of 60,000 IU of cholecalciferol for 16 weeks [15]. The use of all medicines related to pancreatitis treatment including pancreatic enzymes was discontinued prior to the initiation of the Ayurvedic treatment protocol. Diabetic and hypertensive patients were allowed to continue their respective medications under medical supervision.

Noticeable symptomatic improvement could be seen in first three weeks of the initial residential treatment. After the three-week

Table 1
Demography and disease presentation

	Patients (n = 151)
Age, categories	
<12 years	23 (15.23%)
≥12 years	128 (84.77%)
Age, Mean	24.9 ± 12.1 years
Age, Range	3–62 years
Gender[#]	
Female	49 (32.45%)
Male	102 (67.55%)
Past history (in years), Range	1 month to 24 years
Symptoms	
Abdominal pain	147 (97.35%)
Vomiting	125 (82.78%)
Indigestion	149 (98.67%)
Anorexia	67 (44.37%)
Weight loss	115 (76.15%)

Table 2
Details of formulations prescribed

Formulation	Daily Dose	*Anupan*
Amar Capsule	4 mg/kg body weight, divided into three doses	Protein rich diet/ *malai*
Prak-20 Capsule	60 mg/kg body weight, divided into three doses	Water
Rason Vati Tablet	500 mg, 1–2 tablets thrice after meals	Warm water
Chitrakadi Vati Tablet	250 mg, 1–2 tablets thrice before meals	Without water
Kamdudha Ras Powder	125 mg, twice or thrice 15 min before meals	*Mishri*
Sootshekhar Ras Tablet	250 mg, 1–2 tablets twice a day on empty stomach	Water
Narikel Lavan Powder	1 gm, once-twice a day on empty stomach	Buttermilk
Hingwastak Churna	250–500 mg, thrice a day after meals	Warm water

residential treatment phase, patients were discharged with a month's supply of prescribed medication. Subsequently, regular communication between the medical team and patients was maintained through phone or email, facilitating monthly adjustments of medication regimens based on symptom progression, weight changes, and laboratory results. This remote patient management strategy ensured continued effective care, especially when in-person visits were challenging.

Post-completion of the Ayurvedic Treatment Protocol (ATP), patients underwent comprehensive evaluations to assess their progress on physical, pathological, and radiological levels. This data was instrumental in determining the efficacy of the treatment, involving a comparison of patients' pre-treatment conditions with their outcomes post ATP completion.

2.1. Statistical analysis

Statistical analysis was performed on patients who completed one year-long Ayurvedic treatment. Data was presented in terms of mean ± SD, median, percentiles, or range for continuous variables and percentage for categorical variables. The pre-and post-frequency and intensity of attacks and emergency hospitalizations analysis were done using the SAS 9.4 software (Willcoxon two-sample *t*-test and Mann-Whitney u test).

3. Observations

Out of the 151 patients enrolled, 31% (n 50) were diagnosed for HP based on their genetic tests and the diagnosis of the other 69% (n 101) was based on family history of Pancreatitis.

The age distribution across the patient cohort exhibited a wide demographic range, spanning from 3 to 62 years. Additionally, the duration of their respective illness histories demonstrated considerable heterogeneity, encompassing recorded durations ranging from 1 month to 25 years.

The demographics of enrolled patients provide valuable insights into the prevalence of HP with notable concentrations in Maharashtra (18 cases), Uttar Pradesh (15 cases), and Telangana (13 cases). Interestingly, contrary to the popular belief, the incidence of HP was more seen among individuals who did not consume alcohol (79.5% non alcoholics) or tobacco (88% non tobacco users). Among the patients who consumed alcohol, 61.3% were occasional drinkers (<6 times in a year) and 38.7% were regular users (>500 ml per week). Also, 54% patients were vegetarians. As per their reports, three patients had gall stones and six had sludge in gall bladder, while, six patients had undergone cholecystectomy before opting for Ayurvedic treatment. No known etiology could be established in the other patients.

Among the 151 patients, 88 individuals with a mean age of 23.11 ± 11.63 years completed the Ayurvedic Treatment Protocol (ATP), leading to a significant improvement in their quality of life, marked by a life free from pain and other symptoms. Meanwhile, 41 patients opted to discontinue treatment for various reasons, six patients enrolled for the ATP but did not commence treatment and one patient died due to Dengue fever during the treatment period. 15 patients continue to receive the treatment. The positive impact of the yearlong Ayurvedic treatment is evident in the subset of patients who completed it (n = 88), with the longest disease-free survival reaching 22 years for the first patient enrolled in 2001. While, the last patient in this series was enrolled in July 2023 and is under treatment with no symptoms for two months. The statistically significant reduction of 98.7% in emergency hospital admissions and a notable 92.8% reduction in attack frequency ($p < 0.0001$), highlight the efficacy of the treatment. Flow chart of the patient disposition has been depicted in Fig. 1.

This outcome was successfully attained even after the cessation of pancreatic enzymes upon initiating ATP. Notably, no patients documented any instances of adverse effects, thus suggesting a high degree of tolerability for the Ayurvedic treatment. Moreover, on conducting a comprehensive comparative analysis of radiological images acquired before and after the treatment, no indications of disease progression have been identified among these patients.

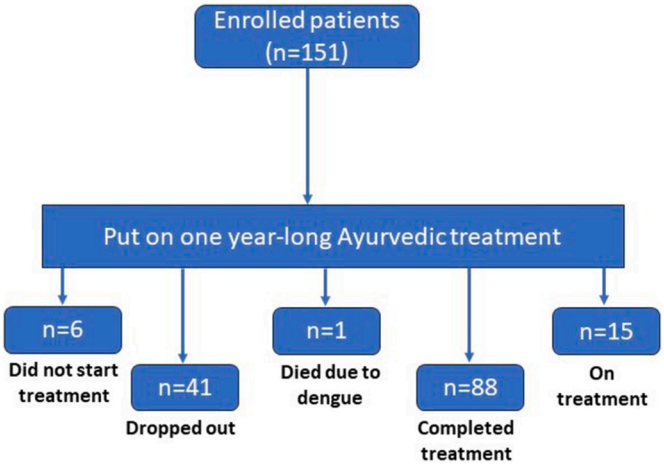

Fig. 1. Flow chart of enrolled patients.

4. Discussion

Hereditary Pancreatitis, characterized by genetic mutations, shares several overlapping symptoms with other forms of pancreatitis [16]. This study delves into the efficacy of a yearlong Ayurvedic treatment protocol in managing Hereditary Pancreatitis (HP), a condition characterized by recurrent and chronic inflammation of the pancreas, often associated with specific gene mutations.

Ayurveda, originating from India, is a traditional medical system that adopts a holistic approach to health and well-being. It employs a range of natural therapies, including dietary adjustments, herbal remedies, and lifestyle modifications, to restore equilibrium in the body and support normal digestive functions and overall health.

The present study's methodology involves the treatment of a diverse patient group consisting of 151 individuals of varying ages and both genders. The treatment protocol used a Metal-Based Ayurvedic Formulation (MBAF) named Amar, supplemented by supportive Ayurvedic formulations and dietary modifications.

Amar, derived from *Rasa-Shastra*, a specialized branch of Ayurveda focusing on Mercury, metals, and minerals, is prepared through a meticulous process involving Copper, Mercury, and Sulphur. Lemon juice and aqueous extracts of *Luffa echinata* and *Clitoria ternatea* are used in its processing. We can say that it is an amalgamation of two principles. Copper has been mentioned as *"Shoth Nashak"* but toxic in nature. Mercury is described to process copper and sulphur *(Gandhak)* is described to eliminate the toxic nature of Mercury by following the concept of *Gandhak Jarana*. Repeated *Jarana* leads to *Jeerna* stage of mercury which possesses *Rog nashak* properties. This is very briefly quoted but not explained in Rasa Tarangini and other texts of rasa shastra. Late Vaidya Chandra Prakash, father of the author, put both concepts together in early seventies and could evolve the formula of AMAR. This formulation, requiring a three-year processing duration, showcases remarkable potential in yielding therapeutic benefits in pancreatic disorders [17].

Results of the study present promising prospects, with 88 patients successfully completing the yearlong Ayurvedic Treatment Protocol (ATP) and experiencing noteworthy enhancement in their quality of life. These individuals reported being free from pain and resuming normal activities.

Geographical distribution analysis highlights a higher prevalence of HP in specific Indian states, notably Maharashtra and Uttar Pradesh. This observation might imply genetic predispositions or environmental

factors influencing disease incidence. The study also underscores lifestyle-related aspects, with a majority of patients being non-alcoholics and non-tobacco users.

A key finding of the study lies in the substantial reduction of attack frequency and emergency hospitalizations following Ayurvedic treatment. Remarkably, these improvements persisted even after discontinuing pancreatic enzyme use, suggesting the Ayurvedic approach's potential to impact underlying disease mechanisms. The Ayurvedic intervention exhibited a favorable safety profile, devoid of reported adverse effects or complications. Radiological evaluations pre- and post-treatment displayed no signs of disease progression in patients who completed the ATP, indicating a stabilization of pancreatic health.

Additionally, the study's extended-term results, depicted through the symptom-free survival curve, illustrate that HP patients could experience disease-free intervals of up to 22 years. This suggests the possibility of utilizing Ayurvedic medicine to extend symptom-free periods for individuals with Hereditary Pancreatitis.

5. Conclusion

In summary, this study underscores the potential merits of Ayurvedic treatment, particularly the Metal-Based Ayurvedic Formulation (MBAF), in the management of Hereditary Pancreatitis. The substantial reduction in the frequency of pancreatitis attacks, coupled with the absence of adverse effects and the lack of disease progression among all treated patients, signifies that the Ayurvedic protocol holds promise as an adjunctive or alternative therapeutic avenue for individuals dealing with HP. However, to substantiate its efficacy and unravel its mechanisms of action, further exploration through randomized controlled trials is imperative. This study offers valuable insights into the management of Hereditary Pancreatitis, shedding light on the viability of Ayurvedic interventions in addressing intricate genetic disorders.

Details of Ayurveda treatment

Ayurvedic Treatment	
Diet *(Aahar)*	1600–2200 calories daily balanced diet divided into three meals and three snacks. Each patient is prescribed protein following age and weight guidelines.
Lifestyle *(Vihaar)*	Eight hours of sleep at night. Avoiding physical and mental exertion.
Medicines *(Aushadh)*	AMAR 4 mg/kg body weight/day, divided into three doses with each meal. Other medicines are given based on patients' symptoms.
Making of AMAR	
Copper (*Tamra*), Mercury *(Parad)* and Sulphur *(Gandhak)* are the main ingredients of AMAR. The process begins with *shodhan* (purification)of the raw materials. *Shodhit* Copper and Mercury and ground into fine powder form. This powder is then ground with *Shodhit Gandhak* by adding liquid extract prepared using lemon juice, *Aprajita* and *Devdali* until the material attains particle size of <5μ at 40X (Checked using particle size analyser). The paste is then made into small pellets and sun dried. After drying, the pellets are subjected to continuous cooking on fire in sealed glass coated clay pots (*nalika damru yantra)* at 360–400 °C.. After cooling, it is again wet ground agin with added Sulphur using lemon juice. The compound is then again subjected to *gandhak jarana.* Gradually same amount of Sulphur takes more time to evaporate and Sulphur nearly two times the quantity of Mercury remains stable on fire inspite of long cooking hours, which has increased from 12 to 120 hours constant cooking. This is described at *dwiguna gandhak jeerna parad* in Ayurvedic texts. The cycle is repeated 100 times with the fire exposure gradually increasing in each cycle for about 3 years. Non destructive analysis using XRD has depicted that 100 times gandhak jarit formulation does not possess any trace of free metals.	
Liquid used in grinding is made of Lemon juice, *Aprajita (Clitoria ternatea)*, *Devdali (Luffa echinate)*. 16 L lemon juice with 1 kg *Aprajita* and *Devdali* each is prepared. 1.8–9 L of this juice is usually consumed during each grinding. The juice consumption gradually increases in each cycle.	

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Author contribution

VBP: Conceptualization, study design, validation, resources, data curation, writing, supervision and project administration. SP: Conceptualization, study design, investigation, review and editing, supervision, project administration. NN: Formal analysis and writing. STS: Formal anlysis and review and editing

Data Statement

All data mentioned in the manuscript is available with the authors and can be presented on request.

Declaration on use of generative AI in scientific writing

None

Conflict of interest

Authors declare no conflicts of competing interest.

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References

[1] Raphael KL, Willingham FF. Hereditary pancreatitis: current perspectives. Clin Exp Gastroenterol 2016 Jul 26;9:197–207. https://doi.org/10.2147/CEG.S84358.

[2] Sahin-Tóth M. Genetic risk in chronic pancreatitis: the misfolding-dependent pathway. Curr Opin Gastroenterol 2017 Sep;33(5):390–5. https://doi.org/10.1097/MOG.0000000000000380.

[3] Shelton C, Solomon S, LaRusch J, et al. PRSS1-Related hereditary pancreatitis [Updated 2019 Apr 25]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [internet]. Seattle (WA): University of Washington, Seattle; 2012 Mar 1. p. 1993–2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK84399/.

[4] Shelton CA, Grubs RE, Umapathy C, Yadav D, Whitcomb DC. Impact of hereditary pancreatitis on patients and their families. J Genet Counsel 2020 Dec;29(6):971–82. https://doi.org/10.1002/jgc4.1221.

[5] Weiss FU. Pancreatic cancer risk in hereditary pancreatitis. Front Physiol 2014 Feb 20;5:70. https://doi.org/10.3389/fphys.2014.00070.

[6] Rebours V, Boutron-Ruault MC, Jooste V, Bouvier AM, Hammel P, Ruszniewski P, Lévy P. Mortality rate and risk factors in patients with hereditary pancreatitis: uni- and multidimensional analyses. Am J Gastroenterol 2009 Sep;104(9):2312–7. https://doi.org/10.1038/ajg.2009.363.

[7] Gross JB, Jones JD. Hereditary pancreatitis: analysis of experience to may 1969. The Exocrine Pancreas; 1969. p. 247–70.

[8] Lowenfels AB, Maisonneuve P, DiMagno EP, Elitsur Y, Gates Jr LK, Perrault J, Whitcomb DC. Hereditary pancreatitis and the risk of pancreatic cancer. International hereditary pancreatitis study group. J Natl Cancer Inst 1997 Mar 19;89(6):442–6. https://doi.org/10.1093/jnci/89.6.442.

[9] Srinivasan G, Venkatakrishnan L, Sambandam S, Singh G, Kaur M, Janarthan K, John BJ. Current concepts in the management of acute pancreatitis. J Fam Med Prim Care 2016 Oct-Dec;5(4):752–8. https://doi.org/10.4103/2249-4863.201144.

[10] Singh NK, Sengar AS, Khuntia BB, Meena AK, Babu G. Management of recurrent attacks of pancreatitis through Ayurveda. Int J Ayurveda Res 2022;3(2):148–52. https://doi.org/10.4103/ijar.ijar_9_22.

[11] Prakash VB, Prakash S, Sharma S, Tiwari S. Relevance of metal-based ayurvedic formulations in the management of recurrent acute/chronic pancreatitis. HUMANITAS MEDICINE 2017;7(2):9–10. https://doi.org/10.5667/tang.2017.0007.

[12] Prakash VB, Prakash S, Sharma S, Tiwari S. Impact evaluation of ayurvedic treatment protocol on three hundred nineteen cases of different variants of pancreatitis. Pancreatic Disorders and Therapies 2018;8(2). https://doi.org/10.4172/2165-7092.1000196.

[13] Savrikar SS, Ravishankar B. Introduction to 'rasashaastra' the iatrochemistry of Ayurveda. Afr J Tradit, Complementary Altern Med 2011;8(5 Suppl):66–82. https://doi.org/10.4314/ajtcam.v8i5S.1.

[14] Sur D, Saha DR, Manna B, Rajendran K, Bhattacharya SK. Periodic deworming with albendazole and its impact on growth status and diarrhoeal incidence among children in an urban slum of India. Trans Roy Soc Trop Med Hyg 2005;99(4): 261–7. https://doi.org/10.1016/j.trstmh.2004.08.005.

[15] Brustad N, Yousef S, Stokholm J, Bønnelykke K, Bisgaard H, Chawes BL. Safety of high-dose vitamin D supplementation among children aged 0 to 6 years: a systematic review and meta-analysis. JAMA Netw Open 2022;5(4):e227410. https://doi.org/10.1001/jamanetworkopen.2022.7410.

[16] Rosendahl J, Bödeker H, Mössner J, Teich N. Hereditary chronic pancreatitis. Orphanet J Rare Dis 2007 Jan 4;2:1. https://doi.org/10.1186/1750-1172-2-1.

[17] Prakash VB, Prakash S, Sharma S, Tiwari S. Transformation of copper into therapeutic mineral complex following principles of rasa shastra. Annals Ayurvedic Med 2020;9(3):162–70. https://doi.org/10.5455/AAM.114202.