Published online in http://ijam.co.in ISSN No: 0976-5921

International Journal of Ayurvedic Medicine, Vol 14 (4), 2023; 1007-1014

Accelerated Stability Study of *Kailas Jeevan* – A Proprietary *Ayurvedic* formulation

Research Article

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Abstract

Background: Stability studies are the test to assess the shelf life of *Ayurvedic* proprietary medicines. Govt. of India made mandatory tests for the licensing and renewal of licensing of proprietary medicine. Accelerated stability studies, testing interval of 0,3, and 6 months. *Kailas Jeevan* is a proprietary semisolid dosage form prepared in GMP-approved Ayurveda Sumshodanalaya (P) Pvt. Ltd. Dhayri, Pune. It is indicated in Constipation, Cracked heels, Wounds, Pimples, Burns, etc. Aims and Objectives: To evaluate the shelf life of *Kailas Jeevan* through accelerated stability study. Materials and Methods: The formulation was prepared in the GMP-approved pharmacy. The product's Shelf life was evaluated by assessing changes in physicochemical, Microbial, and quantification profiles, after keeping it in a stability chamber at a specific temperature (40±2°C) and relative humidity (75±5%). Analysis was carried out at the intervals of 0, 1, 3, 6, 9,12, 18 and 24 months. An average 25% degradation time was calculated to find the shelf life as per the *Ayurvedic* Pharmacopoeia of India, Part I Vol ix guidelines. Results and Conclusion: The parameters assessed in the accelerated study of *Kailas Jeevan,* was shown under limits till 24 months. Based on the multiplication factor shelf life of *Kailas Jeevan* is 7.02 years.

Keywords: Stability, Shelf life, Kailas Jeevan, Accelerated stability study.

Introduction

Stability studies are the shelf life determining studies. The study methodology is available in different guidelines like World Health Organisation (WHO) (1), and International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) guidelines (2). The Govt. of India and, the Ministry of Ayush also accepted stability studies for all the licensed ASU medicines and guidelines are available in Ayurvedic Pharmacopoeia of India (API) Part I, Vol IX (3). These guidelines are mainly intended for manufacturers who wish to assign a shelf life longer than one specified by the Govt. of India. The guidelines can be used for all patented and Proprietary Ayurvedic medicines, both existing and New ones.

Kailas Jeevan is a proprietary semisolid dosage form, commonly used in Fissures, Constipation, Burning sensation of urine, palms, soles, and eyes, Cracked heels, Prickly heat, wounds, Pimples, and burns. It is composed of *Narikela taila* (Coconut oil), *Shweta Raal* (resin of *Shorea robusta*), *Chandana taila* (oil of *Santalum Album*), *Karpura, Kadunimba, Gokharu, Doorva, Pahaadamoola, Shankhajira,* and *Sudhajala.* The formulation has been in the market for many years as a famous brand in the name of multipurpose Ayurvedic cream. As per the new amendment, the pharmacies manufacturing proprietary medicine should provide a stability report to continue the license. So, an accelerated Stability study was undertaken. There is no competing interest. *Kailas Jeevan* is not a patented formulation but it is a proprietary approved formulation, the Pharmacy and authors are interested in publishing the data.

In the present study, we framed the stability study testing protocol not diluting the guidelines. The protocol is framed based on the type of formulation, individual for all proprietary medicines. These guidelines include testing the product's Physical, Chemical, Microbiological, and Chemical quantification. Testing all these parameters is easy in single-entity formulation but multi-drug formulation is very difficult to set. Hence, we framed the pre-zero study plan and executed the study in a simple protocol. The accelerated study gives early outcomes to the pharmacy to test the stability of different products.

In the present study, three primary batches were tested for all the parameters, and quantification like total phenolic content was selected as this formulation is multi-drug keeping this in mind. The testing of the

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product was carried out at 1 month also to ensure the quality of the product. Then further study was conducted to calculate the degradation value.

Materials and Methods

- **Preparation of test drug:** The formulation was prepared in the GMP-approved pharmacy, Ayurved Samshodhanalaya (P) Pvt. Ltd. Dhayri, Pune – 411041. India. License Number PD/AYU/25.
- **Sample quantity and packing:** The 120 gm of formulation was packed in polyethylene containers.
- **Batches and Number of Samples:** Three primary batches were selected for the study. From each batch 12 samples (8 samples for the testing and 4 samples were kept for the cross checking) were collected and kept in a Stability chamber.
- **Study period:** The study was conducted between November 2019 to November 2021.
- **Storage conditions in the stability chamber:** The accelerated stability was conducted following the API guidelines. The temperature was maintained at 40±2°C, while the relative humidity was 75±5%.
- **Frequency of withdrawal of the sample:** The sample was withdrawn from the stability chamber at the intervals of 1, 3, 6, 9, 12, 18, and 24 months and evaluated for relevant parameters.
- **Physiochemical analysis:** The formulation was studied at the specified intervals for changes in organoleptic parameters like color, odor, and form and physicochemical parameters like Rancidity (4), Loss on drying (5), Spreadability (6), Fat content (7), Diethyl ether and Alcohol soluble extracts (8), pH, in quantitative assay total phenolic content (9) and tests for microbial contamination (10).
- **Preparation of Sample for Phytochemical Analysis:**
- The diethyl ether extract was prepared as per the API reference (8). The phytochemical tests were conducted as per Khandelwala (11), the detailed methods and observations are attached in Appendix I.

Observations and Results

The product was analyzed for analytical parameters initially and after storing under the specific conditions for 1, 3, 6, 9, 12, 18, and 24 months. The observations of Organoleptic, Physicochemical, Assay and Quantification of all batches with different intervals were tabulated.

Table 1: Organoleptic characters

	Batch 1			Batch 2			Batch 3		
Months	**Form**	**Color**	**Odor**	**Form**	**Color**	**Odor**	**Form**	**Color**	**Odor**
0 month	Semisolid	Dark creamish	Characteristic	Semisolid	Dull creamish	Characteristic	Semisolid	Dull creamish	Characteristic
1 month	Semisolid	Dark creamish	Characteristic	Semisolid	Dull creamish	Characteristic	Semisolid	Dull creamish	Characteristic
3 month	Semisolid (A little oil layer is formed)	Creamish	Characteristic	Semisolid (A little oil layer is formed above)	Creamish	Characteristic	Semisolid (A little oil layer is formed above)	Creamish	Characteristic
6 month	Semisolid (0.1 cm oil layer is formed above)	Creamish brown	Characteristic	Semisolid	Creamish	Characteristic	Semisolid (0.2 cm small oil layer is formed above)	Creamish brown	Characteristic
9 month	Semisolid(Little oily appearance on upper layer)	Creamish	Characteristic	Semisolid (Little oily appearance on upper layer)	Creamish	Characteristic	Semisolid(Little more oily appearance on upper layer)	Creamish	Characteristic
12 month	Semisolid(Little oily appearance on upper layer)	Creamish	Characteristic	Semisolid(Little oily appearance on upper layer)	Creamish	Characteristic	Semisolid(Little more ++oily appearance on upper layer)	Creamish	Characteristic
18 month	Semisolid	Creamish yellow	Characteristic	Semisolid	Creamish yellow	Characteristic	Semisolid	Creamish yellow	Characteristic
24 month	Semisolid	Creamish yellow	Characteristic	Semisolid	Creamish yellow	Characteristic	Semisolid	Creamish yellow	Characteristic

Table 2: Extractive value of Batch 1

Tests	**Alcohol Extract**				**Diethyl ether Extract**			
	0 month	**1 month**	**3 month**	**6 month**	**0 month**	**1 month**	**3 month**	**6 month**
Carbohydrates	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve
Reducing sugar	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Monosaccharides	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Pentose Sugar	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Non reducing sugar	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve

Hexose Sugar	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Proteins	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Amino Acids	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Steroids	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve
Flavonoids	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve
Alkaloids	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Tannins	+ve	+ve	+ve	+ve	-ve	-ve	-ve	-ve
Cardiac Glycosides	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve
Anthraquinone glycosides	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Saponin Glycosides	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve

Note: The phytochemical study of all 3 batches shown same results

Table 3: Loss on drying

	Loss on Drying		
Months	**Batch 1**	**Batch 2**	**Batch 3**
0 month	8.187%	8.3%	9.037%
1 month	9.491%	9.452%	9.362%
3 month	10.242%	9.635%	8.56%
6month	8.893%	10.193%	9.304%
9 month	8.812%	10.594%	9.903%
12 month	10.89%	10.776%	9.489%
18 month	7.677%	8.6%	9.811%
24 month	8.633%	9.25%	10.507%

Graph 1: Loss on drying

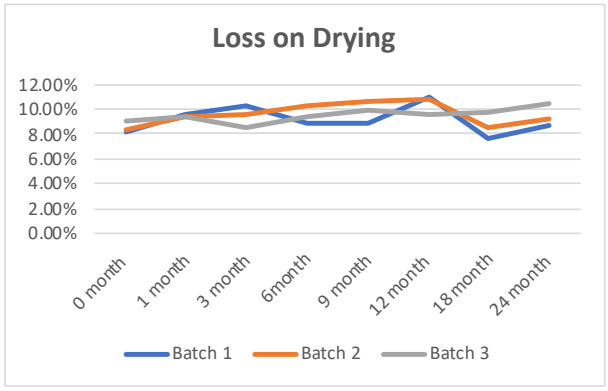

Table 4: pH Value

	pH Value		
Months	**Batch 1**	**Batch 2**	**Batch 3**
0 month	8.40	8.45	8.45
1 month	7.81	7.64	8.15
3 month	7.89	7.72	7.95
6month	6.87	6.32	6.57
9 month	6.30	6.08	6.40
12 month	6.71	6.13	6.26
18 month	7.83	7.85	7.71
24 month	7.47	7.38	7.64

Graph 2: pH Value

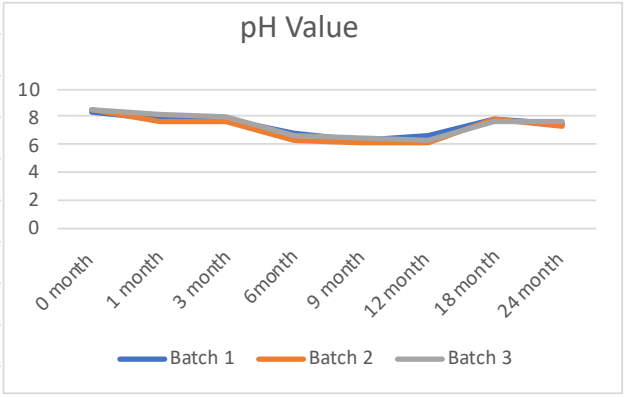

Table 5: Alcohol soluble extractive value

	Alcohol soluble extractive value		
Months	**Batch 1**	**Batch 2**	**Batch 3**
0 month	32.006%	32.378%	30.710%
1 month	27.919%	30.365%	26.38%
3 month	28.577%	26.962%	27.466%
6month	24.075%	23.525%	22.672%
9 month	24.938%	26.277%	24.697%
12 month	23.934%	23.648%	24.315%
18 month	26.267%	26.97%	28.667%
24 month	33.609%	33.165%	31.686%

Graph 3: Alcohol soluble extractive value

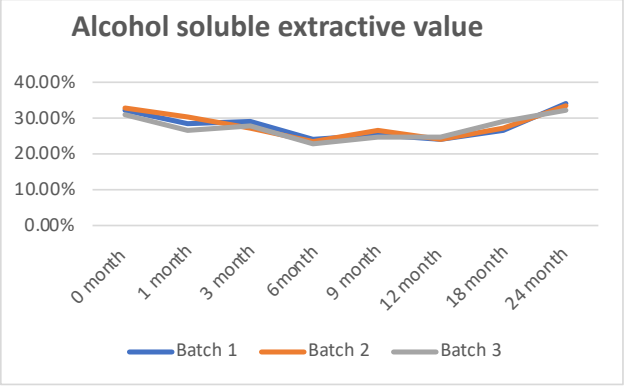

Table 6: Diethyl Ether Soluble Extractive Value

	Diethyl Ether Soluble Extractive Value		
Months	**Batch 1**	**Batch 2**	**Batch 3**
0 month	31.901%	36.193%	33.523%
1 month	33.523%	34.055%	32.520%
3 month	32.251%	34.592%	33.519%
6month	31.303%	32.191%	30.566%
9 month	32.874%	35.314%	33.946%
12 month	32.522%	33.070%	32.375%
18 month	32.404%	34.675%	30.893%
24 month	37.784%	40.203%	38.594%

Graph 4: Diethyl Ether Soluble Extractive Value

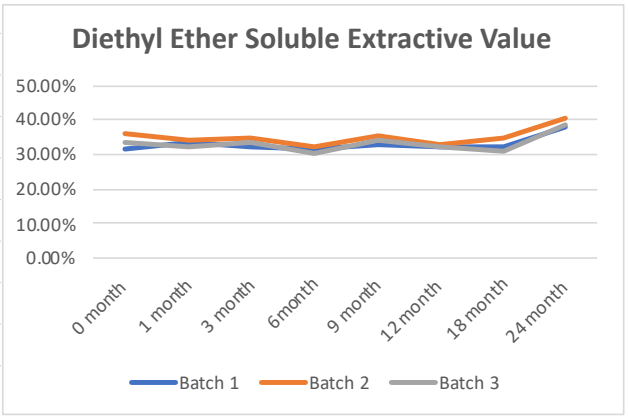

Table 7: Spreadability in mm

	Spreadability in mm		
Months	**Batch 1**	**Batch 2**	**Batch 3**
0 month	36	37	38
1 month	32	34	40
3 month	37	37	34
6month	37	37	34
9 month	42	40	39
12 month	40	42	42
18 month	46	40	44
24 month	44	42	47

Graph 5: Spreadability test

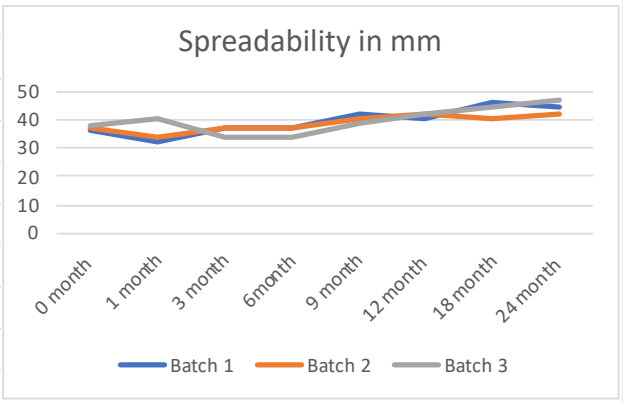

Table 8: Fat content

	Fat content		
Months	**Batch 1**	**Batch 2**	**Batch 3**
0 month	14.19%	17.40%	17.93%
1 month	11.11%	15.15%	15.37%
3 month	10.68%	7.85%	9.25%
6month	12.68%	16.92%	13.67%
9 month	14.46%	17.11%	16.98%
12 month	14.63%	15.56%	15.62%
18 month	16.402%	18.007%	17.587%
24 month	17.308%	21.112%	21.348%

Graph 6: Fat content

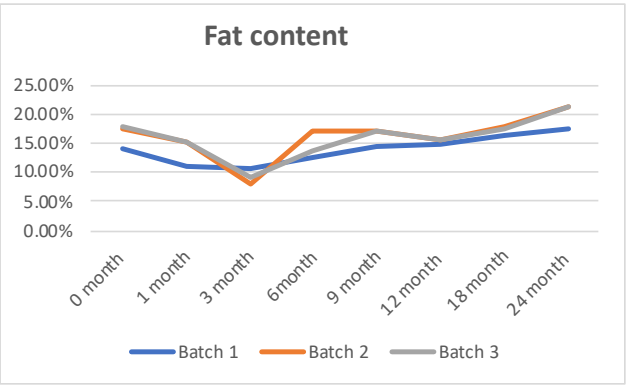

Table 9: Phenolic content

	Phenolic content in mg GAE/gm of Extract		
Months	**Batch 1**	**Batch 2**	**Batch 3**
0 month	9.14±0.13	10.02±0.11	9.60±0.54
1 month	8.94±0.40	7.47±0.39	8.83±0.40
3 month	7.05±0.56	6.41±0.23	7.05±0.24
6month	7.96±0.37	8.04±0.48	8.84±0.40
9 month	8.24±0.51	7.34±0.53	7.1±0.24
12 month	8.5±0.26	7.71±0.33	7.0±0.19
18 month	7.88±0.37	8.94±0.27	10.21±0.43
24 month	8.73±0.39	8.29±0.42	9.68±0.35

Graph 7: Phenolic content

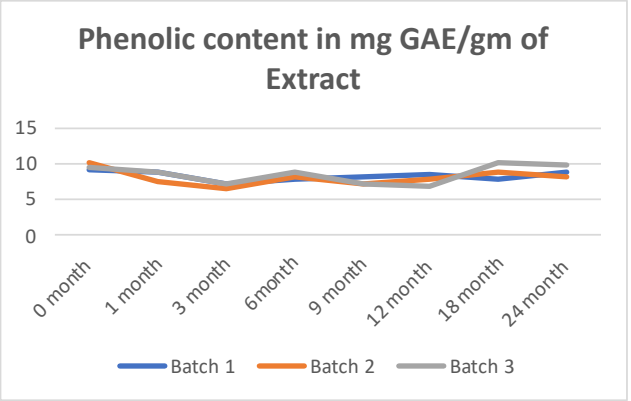

Table 10: Total Microbial Growth: Batch 1

Test Attributes		Duration							
Test for specified Micro-Organisms (Qualitative)	**Limits (As per IP)**	**0 month**	**1 month**	**3 month**	**6 month**	**9 month**	**12 month**	**18 month**	**24 month**
E coli	Absent/100ml	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
S aureus	Absent/100ml	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
P aeruginosa	Absent/100ml	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
S Abony	Absent/100ml	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Microbial limit test(Quantitative)									
Total Bacterial Count	30 - 300 cfu/ml	07 cfu/ml	19 cfu/ml	13 cfu/ml	18 cfu/ml	06 cfu/ml	09 cfu/ml	08 cfu/ml	12 cfu/ml
Total Fungal Count	10 - 100 cfu/ml	03 cfu/ml	03 cfu/ml	02 cfu/ml	02 cfu/ml	02 cfu/ml	01 cfu/ml	04 cfu/ml	07 cfu/ml

Table 11: Total Microbial Growth: Batch 2

Test Attributes		Duration							
Test for specified Micro-Organisms	**Limits (As per IP)**	**0 month**	**1 month**	**3 month**	**6 month**	**9 month**	**12 month**	**18 month**	**24 month**
E coli	Absent/100ml	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
S aureus	Absent/100ml	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
P aeruginosa	Absent/100ml	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
S Abony	Absent/100ml	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Microbial limit test(Quantitative)									
Total Bacterial Count	30 - 300 cfu/ml	08 cfu/ml	17 cfu/ml	17 cfu/ml	18 cfu/ml	09 cfu/ml	08 cfu/ml	06 cfu/ml	16 cfu/ml
Total Fungal Count	10 - 100 cfu/ml	03 cfu/ml	04 cfu/ml	08 cfu/ml	08 cfu/ml	01 cfu/ml	02 cfu/ml	03 cfu/ml	08 cfu/ml

Table 12: Total Microbial Growth: Batch 3

Test Attributes		Duration							
Test for specified Micro – Organisms	**Limits (As per IP)**	**0 month**	**1 month**	**3 month**	**6 month**	**9 month**	**12 month**	**18 month**	**24 month**
E coli	Absent/100ml	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
S aureus	Absent/100ml	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
P aeruginosa	Absent/100ml	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
S Abony	Absent/100ml	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Microbial limit test(Quantitative)									
Total Bacterial Count	30 - 300 cfu/ml	08 cfu/ml	24 cfu/ml	18 cfu/ml	28 cfu/ml	09 cfu/ml	07 cfu/ml	11 cfu/ml	17 cfu/ml
Total Fungal Count	10 - 100 cfu/ml	02 cfu/ml	06 cfu/ml	09 cfu/ml	09 cfu/ml	01 cfu/ml	03 cfu/ml	06 cfu/ml	08 cfu/ml

Table 13: Intercept and slope

Parameters	Batch 1		Batch 2		Batch 3	
	Slope	**Intercept**	**Slope**	**Intercept**	**Slope**	**Intercept**
Loss on Drying	-0.03087	9.384843	-0.03267	9.596873	0.058179	8.965737
pH Value	-0.02137	7.605016	-0.01962	7.375293	-0.02631	7.631292
Alcohol soluble extractive	0.058495	27.13374	0.032852	27.61397	0.116868	26.009829
Diethyl Ether Soluble Extractive Value	0.158718	31.6192	0.152501	33.64468	0.130899	32.04805
Spreadability in mm	0.478831	34.88066	0.276058	36.10597	0.434266	35.78732
Fat content	0.234683	11.79102	0.264668	13.72353	0.254625	13.64592
Phenolic content in mg GAE/gm of Extract	-0.00177	8.321176	0.014642	7.89389	0.046925	8.11056

Table 14: Approximate Period in months for 20% degradation

Parameters	Batch 1		Batch 2		Batch 3	
	20% Degradation	Approx.	20% Degradation	Approx.	20% Degradation	Approx.
Loss on Drying	6.54	30.92	6.64	28.74	7.22	14.70
pH Value	6.72	36.25	6.76	38.26	6.76	29.69
Alcohol soluble	25.6	43.82	25.90	81.56	24.54	21.17
Diethyl Ether Soluble Extractive Value	25.52	17.36	28.95	19.16	26.81	21.81
Spreadability in mm	28.8	4.40	29.6	10.12	30.4	5.20
Fat content	11.35	3.88	13.92	3.79	14.34	3.93
Phenolic content	7.31	47.08	8.01	53.26	7.74	16.51
	Average	**26.24**	**Average**	**33.55**	**Average**	**16.14**

The approximate period in months for degradation is calculated based on intercept and slope. The shelf life was assessed by taking the average month degradation and multiplication with the real-time ageing factor mentioned for India, it comes under zones III and IV.

Table 15: Evaluation of shelf life of *Kailasa Jeevana*

Batch	Month	Multiplication factor	Shelf life	
			Months	Year
1	26.24	3.33	87.37	7.28
2	33.55	3.33	111.72	9.31
3	16.14	3.33	53.74	4.47
	Average		84.27	7.02

Discussion

Recent Ayush Gazette on shelf life studies made mandatory for proprietary ASU medicine has created a lot of problems in pharmacies, because of the complexity of medicine many pharmacies facing difficulty and looking for scientific solutions. To overcome this, we have prepared our protocol by including all the concepts of stability study with a practical approach.

The *Kailas Jeevan* is an *Ayurvedic* proprietary medicine available in the market, indicated for Crack heels, Burn wounds, Stomatitis, etc. for many decades.

Kailasa Jeevan accelerated stability test was performed based on API guidelines. API does not mention similar degradation values for all testing parameters. Storage condition is similar to ICH guidelines but the evaluation is completely based on the parameters tested and its value. As per the standard guidelines mentioned in API for Ayurveda products, there a separate evaluation points given for physicochemical, TLC, and active ingredients of the formulation may be due to multiple ingredients in a single formulation.

In modern pharmaceutics, quantification is based on the assay of Active pharmaceutical ingredient which is a single molecule but in *Ayurvedic* proprietary medicine it is a multiple ingredients having multiple compounds, which is a challenge to quantify all the ingredients. The present formulation has shown the presence of Phenols in preliminary phytochemicals. Hence we have considered total phenol count as a quantification assay as a representative chemical group through UV Spectrophotometry. In the present study, we were able to conduct an estimation of Total phenols in different time intervals until 24 months and their degradation slope.

As the formulation is fatty media, it has become challenging to do phytochemical analysis, to overcome this we employed different solvent extraction methods and succeeded in analyzing them.

The results of all the parameters were within normal limits as mentioned in degradation, but slight variation seen in each testing interval may be due to temperature and humidity maintained in the stability chamber. The physical and chemical parameters may be changed due to the chemical transformation in the *Kailas Jeevan.*

In this study, we have made the protocol to include physical, chemical, biological, microbial, and pharmaceutical dosage testing.

In the present study, 0-month and First-month analysis was carried out to establish the standard testing protocol for stabilities studies as there is no standard available for the *Kailasa Jeevan*, then based on these analyses the degradation value is calculated. The product was studied for 24 months and there are no changes in its value specified in API. Shelf life calculation is not mentioned in API, but in this study, we have calculated the shelf life by using the multiplication factor i.e. 3.36 mentioned in ICH guidelines. Even though API mentioned a six-month accelerated study here study was extended up to 24 months. *Kailas Jeevan* has not shown degradation below the accepted value of 20%.

High-end analytical techniques like HPTLC, HPLC, and GC may also be used for quantification in a future study with appropriate markers, but in the present study, we could fulfill the guideline using a simple UV Spectrophotometer.

Conclusion

The present study has found that the shelf life of *Kailasa Jeevan* is 7.02 years, according to an accelerated stability study. Our developed protocol based on API guidelines has shown usefulness in the evaluation of complex Ayurvedic formulation.

Acknowledgment: CRF KAHER Shri BMK Ayurveda Mahavidyalaya Belagavi, Ayurved Samshodhanalaya (P) Pvt. Ltd. Dhayri, Pune – 411041.

Financial support and sponsorship:
Ayurved Samshodhanalaya (P) Pvt. Ltd. Dhayri, Pune – 411041.

Conflicts of interest: There are no conflicts of interest.

Appendix I: Method of Organic phytochemical screening

Test	sample	Quantity of reagent	Procedure	Result
Carbohydrate	2-3 ml	Added a few drops of alpha naphthol in alcohol	Shaked and added concentration of H2SO4, From the side of the test tube.	Violet ring at the junction of two liquids
Reducing sugar	3ml	3ml benedicts reagent added	Heated in a water bath for 5 min	Green Yellow or Red depending on the amount of reducing sugar
Monosaccharides	2ml	2ml Barfoeds reagent	Heated in a water bath for 1-2min and cool	Red ppt
Pentose sugar	Few Drop	3ml of Bial's reagent	Boiled the reagent and added a few drops of sample	Green or purple color
Hexose sugar	1ml	3ml selwioffs reagent	Heated for 1 to 2 min	Red color
Protein	3ml	5ml Millions Reagent added	White ppt -warm ppt	Turns brick red or ppt dissolved giving red color solution.
Amino acids	3ml	3 drops of 5% Ninhydrin Solution	Heated in Boiling Water bath for 10min	Purple or Bluish color
Steroids	2ml	2ml chloroform and 2ml conc.H2SO4	Shaked well and observed in UV chamber	Chloroform layer-Red Acid layer-Greenish yellow Fluorescence
Flavonoids	A small quantity of extract	Added Lead acetate solution		Yellow color ppt
Alkaloids	2-3ml	Added a few drops of Dragendroff's reagent		Orange-brown ppt
Tannins	2-3ml	Lead acetate solution		White ppt
Cardiac Glycosides	2ml	Glacial acetic acid, 2 drops of 5% Fecl3, and conc.H2SO4		The reddish brown color at the junction of two liquids, upper layer bluish green
Anthraquinone glycosides	3ml	Diluted H2SO4	Boiled and filtered, added equal volume of chloroform. shaked well and separated the organic solvent and added Ammonia	Ammonical layer shows pinkish red color.
Saponin glycosides	3ml	Equal amount of distilled water	Shaked well	Persistence foam

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