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Development and Formulation of Topical Alum Gel by Using Quality By Design

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Abstract:

Topical gels are basically used for both localized medication action and cosmetic/therapeutic uses. Alum (potassium alum) has astringent, deodorant, antibacterial, and skin-soothing characteristics, making it a potential topical formulation ingredient. Because of the diversity in traditional formulations, implementing a systematic Quality by Design (QbD) strategy can assist ensure consistent product quality, performance, and stability. The goal is to create and improve a topical alum gel formulation utilizing a QbD framework, identifying the Quality Target Product Profile (QTPP), Critical Quality Attributes (CQAs), Critical Material Attributes (CMAs), and Critical Process Parameters (CPPs) that influence gel quality and performance. Methods: Define QTPP, identify CQAs, select input variables, Design of Experiments.

Prepare alum gel batches and test their physical qualities (pH, viscosity), rheology, in vitro release, and stability. Results: The QbD-guided formulation enabled the adjustment of critical formulation parameters. The optimal polymer and alum concentration resulted in a gel with an acceptable pH (skin-friendly) and viscosity for easy spreadability. Response surface or contour plots were used to guide the formulation space selection to meet CQA requirements. The improved gel maintained uniform medication distribution and the desired texture. Conclusion: Quality by Design allowed for a more systematic formulation of topical alum gel with predictable and resilient quality features than traditional trial-and-error methods. The improved gel meets prescribed quality requirements and is ready for further evaluation in stability tests or clinical trials.

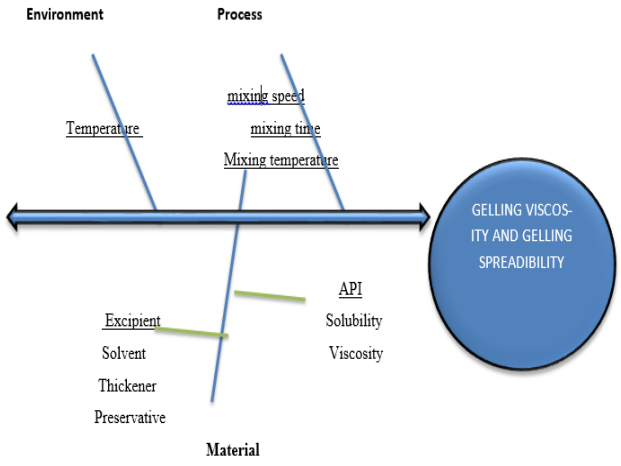
Keywords- Alum Gel, Potassium Aluminum Sulfate, Topical Drug Delivery, Design of Experiments, Formulation Development, CQAs, and Stability Studies.

INTRODUCTION

Topical medication delivery techniques achieve targeted therapeutic benefits while limiting systemic exposure. Basically gels are used because they are non-greasy, easy to apply, cosmetically appealing, and can deliver active substances straight to the affected area.

Alum (potassium aluminum sulfate dodecahydrate) is a naturally occurring double sulfate salt with known antibacterial, astringent, deodorizing, and hemostatic effects. It has long been used to reduce minor bleeding, decrease sweating, and treat superficial skin infections. Incorporating alum into a gel form may increase patient convenience, skin contact time, and product acceptability.

The International Council for Harmonisation



(ICH) promotes Quality by Design (QbD), a science- and risk-based approach to pharmaceutical development. Rather than relying solely on end-product testing, QbD focuses on building quality into the product by extensively understanding formulation variables and manufacturing processes.

The goal of this research was to use the QbD approach to develop and optimize a topical alum gel by identifying formulation and process factors that affect the quality of the final product and creating a strong design space.

MATERIAL AND METHOD:

3.5.Selection of parameters through Ishikawa approach

From this Ishikawa diagram we are selected process parameters and material parameters for our formulation of gel. Which is use for the clotting of blood on the surface of skin, induces by minor or major cuts on the skin.

Selection of polymer with the combination

S.No.	Polymer combinations		Ratio
	Polymer 1	Polymer 2	
1.	Carbopol	Chitosan	1:1
			1:2
			2:1
2.	Sodium alginate	CMC	1:1
			1:2
			2:1
3.	Chitosan	Sodium alginate	1:1
			1:2
			2:1
4.	CMC	Chitosan	1:1
			1:2
			2:1
5.	Carbopol	Sodium alginate	1:1
			1:2
			2:1

Selection of polymer with the alum :

S. No.	Polymer	Concentration (mg)	Solvent (ml)	Alum (%)
1.	Carbopol	1000	Distilled water (50 ml)	1
				0.5
				0.2
2.	Sodium alginate	1500	Distilled water (50 ml)	1
				0.5
				0.2
3.	CMC	1000	Distilled water (50 ml)	1
				0.5
				0.2
				0.15
				0.1
4.	Chitosan	1500	1% Acetic acid (50ml)	1
				0.5
				0.2

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Selection of process parameters

S. No.	Time of stir-ring (min)	Speed of stir-ring (RPM)	Tempera-ture of stir-ring (°c)	Responses
1	15	200	45	Gel was not properly formed
2	20	200	45	Gel was properly formed
3	25	200	45	Gel was formed
4	30	200	45	Gel was formed
5	20	400	45	Gel was formed with slightly high viscosity
6	20	600	45	Gel was formed with optimum viscosity
7	20	800	45	Gel was formed with slightly low viscosity
8	20	600	55	Gel was formed
9	20	600	65	Gel was formed with optimum viscosity
10	20	600	75	Gel was formed with slightly low viscosity

Method of alum gel preparation:

Weighed the excipients and API accurately using a calibrated analytical weighing balance, then took the needed amount of Chitosan (1500 mg) and blended it into 40 ml of distilled water on a magnetic stirrer until uniformly combined. The mixing was then extended for a set period of time. The gel was treated with a preservative (90 mg methyl paraben sodium and 10 mg propyl paraben sodium). After adding 4ml of phosphate buffer (pH 4.5), the gel was neutralized. Then, dispersed 250 mg of potash alum in 6 ml of distilled water combined with the gel.

Design of experiments

A design of experiments was utilized For better understand of formulation and the process. To ensure the production process and its basic characteristics remain stable. A few preliminary investigations were conducted to determine the beginning formulations and factor variation limits.

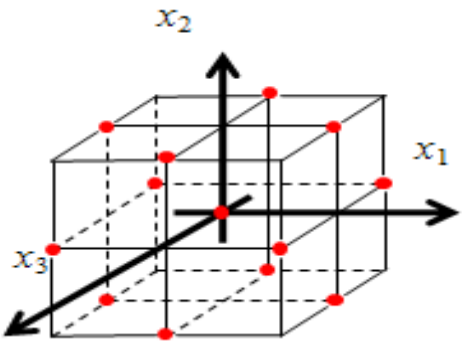

Fig. 3. box-Behnken desi

Generally says, the QbD approach's experimental work demonstrates the entire spectrum of interactions between the selected inputs and the investigated responses. "The multidimensional combination and interaction of input variables that have been shown to offer quality assurance " is the definition of the design space.

Obtained process parameters:

Variable	Range	Variables
	Lower range	Upper range
Stirring time	10 minutes	30
Stirring speed	400 RPM	800
Stirring temperature	45°c	75°c

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Run	Factor 1 A:stiring time min	Factor 2 B:stiring tem... degree celcius	Factor 3 C:stiring speed RPM	Response 1 viscosity centipoise	Response 2 spreadibility gm-cm/min	Response 3 swelling index -
1	20.00	75.00	400.00			
2	20.00	45.00	800.00			
3	10.00	75.00	600.00			
4	30.00	60.00	800.00			
5	10.00	60.00	800.00			
6	20.00	75.00	800.00			
7	30.00	75.00	600.00			
8	10.00	60.00	400.00			
9	30.00	60.00	400.00			
10	30.00	45.00	600.00			
11	20.00	45.00	400.00			
12	10.00	45.00	600.00			

RESULTS AND DISCUSSION:

Trials of gel in combination:

In the formulation of combinations of gel. no gel was formed properly in their combinations, some of them are segregated, separated and some are form plagues. In combination of sodium alginate and CMC the gel was properly formed but after the addition of alum in to them, the gel was separated.

Trial of polymer with alum:

In the trial of polymer with alum Carbopol and sodium are separated and segregated after addition of alum in to it. CMC can form a gel with alum but with minor amount of alum (0.1%). Which will give blood clotting time but too far which is 6 minute 26 second. which almost equal to the normal blood clotting time (8 minutes). at last, the gel was formed with

Chitosan and alum (.5%).

Trial for process parameter

In the trial of process parameters, we found that for 20 minutes, 600 RPM, at 65℃ we can form the gel with optimum viscosity.

Obtained gel from runs:

Fig. 4. Trial 1

Fig. 5. Trial 2

Fig. 6. Trial 3

Fig. 7. Twelve trial run gel formulations.

Spreadibility study:

By spreading 0.5 g of the alum gel over a 2 cm-diameter circle on a glass plate placed on cm graph paper and then another glass plate, the spreadibility of the gel was assessed.

For five minutes, a 100-gram weight was placed on top of the glass plate. After the gel was spread, the circle's circumference was measured.

Spreadibility of gel = M × L / T

Where, M is weight which is placed on plate, L is diameter of circle after spreading the gel, T is time taken for spreadibility.

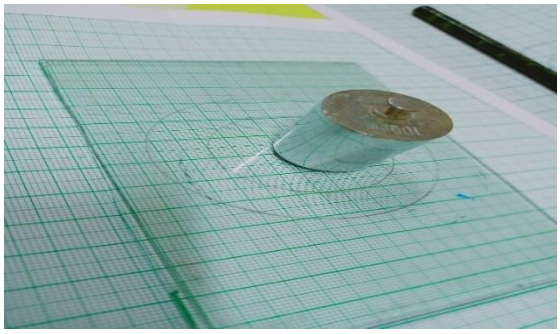

Fig. 8. Spreadibility study test

Viscosity study:

By using the viscometer,the viscosity of the alum gel was measured. The gel was spun at 100 RPM. The dial reading was expressed in centipoise at this speed.

Swelling index:

Bourtoom et al. observed that the test carried out with their methodology Specifically, the dry polymer was initially immersed on measuring balance than it dissolves in distilled water at different RPM for different time, in order to equilibrate them. Then, by heating them at various temperatures, the extra moisture was totally eliminated. Lastly, weighed the samples were, and to determine the degree of swelling by using following formula .

$$\text{Swelling degree (\%)}: \frac{We - Wo}{Wo} \times 100$$

where , Wo is the weight of the dry polymer before to swelling (initial dry weight), whereas We is the weight of the polymer at absorbing equilibrium (fully swelled gel).

Obtained responses after evaluation:

Test tube method for blood clotting time:

1. First, we transferred the gel in the test tube.
2. Tube was set at 37℃ temperatures.
3. Take 4 ml of blood in test tube and start the time.
4. Note the time when first appearance of clotting begins.

Obtained responses after evaluation:

Run	Factor 1 A: stirring time minutes	Factor 2 B: stirring temp. Celsius	Factor 3 C: stirring speed RPM	Response 1 viscosity cent. poise	Response 2 spreadibility g.cm/s	Response 3 Swelling index
1	30.00	45.00	600.00	4949	144	36.3
2	10.00	60.00	400.00	3389	154	37.6
3	30.00	60.00	400.00	3992	164	32.7
4	20.00	75.00	800.00	3275	206	34.9
5	30.00	75.00	600.00	3909	122	31.7
6	10.00	60.00	800.00	6559	126	36.9
7	20.00	75.00	400.00	5969	140	36.4
8	20.00	45.00	800.00	6288	126	36.8
9	10.00	75.00	600.00	5411	128	37.0
10	30.00	60.00	800.00	5447	100	33.5
11	20.00	45.00	400.00	4793	114	36.1
12	10.00	45.00	600.00	5135	120	37.1

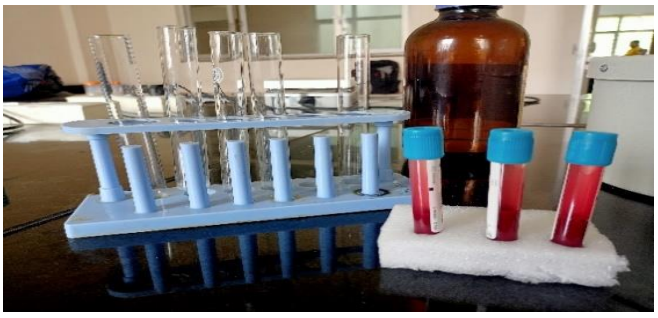

Fig. 11. Test tube method

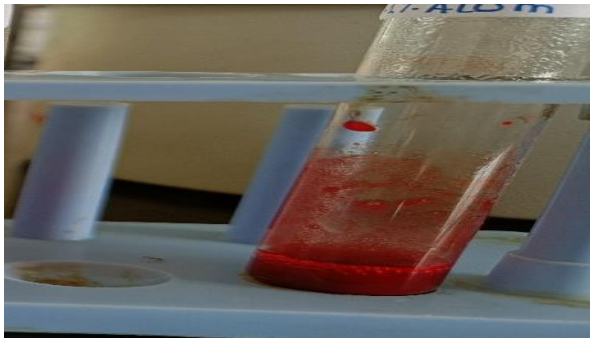

Fig. 12. Blood clotted

	Alum chitosan gel	Marketed (Mancode) gel
Components	API – alum Polymer – chitosan Excipients – methylparaben, 1% acetic acid solution	API – alum Polymer – carbomer Excipients – Aloe vera, menthol, witch hazel, spearmint, etc...
Uses	Blood clotting, wound healing	After shaving gel, moist-urizer, acne remover, etc...
Viscosity	3657 centipoises	3923 centipoises
Spreadibility	132-gram cm/sec	140-gram cm/sec
Blood clotting time	1 minutes 50 second	3 minutes 30 second

SUMMARY AND CONCLUSION:

The current study concluded that chitosan as a polymer can used for formulation of alum gel. It can be use as topical formulation for small or minor cuts on skin. This combination is useful for faster clotting time on open cut. The selection of parameters from box-Behnken design is useful for formation of optimum quality of gel. The formulation gives faster coagulation of blood as comparison to the marketed formulation, because the polymer which we used in formulation is also act as a clotting factor for blood.

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