



Formulation and Evaluation of Pediatric Paracetamol Elixir Using Natural Colorant

Mamatha Tirunagari^{1*}, Nagadivya Nerella¹, Anupama Koneru²,
Madiah¹, Syed Sarfaraz¹, M. A. Mushtaq³

¹Department of Pharmaceutics, Sultan – ul –Uloom College of Pharmacy, Road No: 3, Banjara Hills, Hyderabad – 500034, Telangana State, India

²Department of Pharmacology, Sultan – ul –Uloom College of Pharmacy, Road No: 3, Banjara Hills, Hyderabad – 500034, Telangana State, India

³Department of Pharmacy Practice, Sultan – ul –Uloom College of Pharmacy, Road No: 3, Banjara Hills, Hyderabad – 500034, Telangana State, India

Abstract : Oral dosage forms are most popular among other dosage forms. In terms of bioavailability liquid dosage form is better than that of solid dosage form. In the present scenario monophagic liquid dosage forms such as syrups, elixirs, throat paints, mouth washes, gargles have gained huge popularity. These are very basic preparations which involve brief processes, machineries and are cost effective also. They come in wide range colours and flavors so as to attract the pediatric age group. Currently colors derived from natural sources are given priority compared to synthetic ones. In this study we formulated paracetamol which is a bitter drug as an elixir using natural colorant from annatto seeds at three different concentrations in F1, F2, and F3. Ethanol, Propylene glycol, mixed fruit juice, chloroform spirit, sucrose syrup and glycerin were also used. These formulations were evaluated for different physical parameters and it showed good results.

Keywords : Elixirs, Pediatric, Paracetamol, Monophonic, Annatto, Syrup.

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Running title: Paedriatic Paracetamol Elixir

Introduction:

The word elixir is adopted from Arabic language *al-ʾiksīr* which means magical powder. According to alchemy it turns lead to gold. It is also beloved to be a magical potion which prolongs life span and cures all the ailments and makes a personal eternal. But on the contrary, in pharmaceutical industries it is defined as clear, sweetened hydro alcohol liquids intended for oral use containing flavoring substances or active medicinal agents. They are used either as vehicles or for the therapeutic effect of the medicinal substances that they contain. It is used to mask the unpleasant taste of many drugs and solves many solubility issues of insoluble drugs. Traditionally, water or vegetable oil is used as a suspending agent, although solvent extraction is now also employed to produce more purified annatto extracts. Colouring agent¹ has vital role in all the industries especially in food and pharmaceuticals. Color makes everything very attractive and appealing. Food colors extracted from natural sources like seeds², flowers³, and even algae^{4,5} are good for health whereas use of chemically synthesized artificial color may have side effects⁶ upon long term usage. Wherever there is use of artificial color in food they should be mentioned on the container properly in labeling. Manufacturing companies and industries should strictly follow the guidelines in food laws to ensure the safety and health of the general public. The advantages of natural colorant include Minimal Environmental Impact – Because they come from natural sources, natural dyes are not harmful to the environment, which makes it so appealing for consumers. Natural dyes are biodegradable and disposing them don't cause pollution, Renewable – Natural dyes are obtained from renewable sources that can be harnessed without imposing harm to the environment, Color pay-off – If you're going for a soft hue or soothing shade, natural dyes can help you achieve that look, Safe – Some natural dyes, such as carmine found in lipsticks, will not cause harm or health problems when ingested. The food colour annatto⁷ for the present research work is obtained from the outer layer of the seeds of the tropical tree *Bixaorellana* L.⁸ The principle pigment in annatto, cis-bixin, is a carotenoid, which is contained in the resinous coating^{9,10} surrounding the seed itself. Numerous patents and research reports cover a variety of organic solvents for producing concentrates, such as chlorinated hydrocarbons, mixtures of ethanol and chloroform¹¹, acetone, ethanol, ethyl acetate, hexane, methanol or alcoholic sodium hydroxide. Ingredients in the elixir includes Alcohol¹², Propylene glycol¹³, Glycerin, Preservatives¹⁴, Sucrose syrup, and Flavouring agents. Elixirs have low viscosity than syrups and they can flow more freely as there will be very less use of agents that increase viscosity like sucrose. There is no clear cut difference between elixirs and syrups. To call a formulation as elixir, it must be hydro alcoholic and the amount of alcohol may vary greatly. Elixirs alcohol content, compound benzaldehyde elixir 3 to 5%, aromatic elixir USP 21 to 23%. Glycerin and syrup may also use in the formulation. This enhances the solubility of drug, or to increase the sweet taste. Propylene glycol can also be used as solvent.

Elixirs can be prepared more easily than syrups they contain less amount of ingredients that are to be dissolved. If water soluble and alcohol soluble ingredients are present in formulation then the following procedure is followed. All the water soluble ingredients are added to water and dissolved. Now sucrose should be mixed and let it dissolve completely all the alcohol soluble ingredients were taken and dissolved in alcohol. Then the first solution was added to second solution. To make the elixir clear it is filtered. The final volume is made up with water. Sucrose will enhance the viscosity and reduces the solubility of water. To make the elixir clear which is compulsory, talc or siliceous earth are used. Syrup is the best choice when taste is the main consideration. To make use of reliable, safer and economical natural coloring agents in the preparation of pediatric paracetamol elixir and compare it with the marketed product to evaluate the stability of the color used.

Materials and Methods:

The following product consists of the following drug and excipients. Paracetamol¹⁵ is the choice of drug, ethanol is used as the vehicle (alcoholic portion) an antimicrobial preservative., propylene glycol concentrated mixed fruit juice as flavor, chloroform spirit as preservative, sucrose syrup as sweetener, annatto as natural colorant and glycerin as viscosity modifier.

Table No.1: Formulation Ingredients for Pediatric Paracetamol Elixir

S.No.	Ingredients	General Formula (100 ml)
1	Paracetamol	2.5 gm
2	Ethanol	10 ml
3	Propylene Glycol	10 ml
4	Conc. Mixed Fruit Juice	2.5 ml
5	Chloroform Spirit	2 ml
6	Sucrose Syrup	28 ml
7	Annatto	Different Concentration
8	Glycerin Q.S	Up To 100 ml

Table No.2: Different Concentration of Colorant Added In Elixir

Formulation code	Elixir (ml)	Color added
F1	30	0.0034 %
F2	30	0.034 %
F3	30	0.067 %

Extraction of the natural coloring agent, Annatto:

The fruit is been plucked from the medicinal garden and the seeds are thus removed. The seeds are then weighed accurately and kept for drying .Then the seeds are soaked in ethanol solution and kept aside for 2 days till sufficient amount of color is been extracted. After the sufficient extraction of color filtered the solution and kept the solution for evaporation¹⁶.

Preparation of Elixir:

The paracetamol is weight accurately and is dissolved in measured quantity of alcohol and propylene glycol .To this above mixture, chloroform sprit, concentrated mixed fruit juice and sucrose syrup is added while stirring. This above content is added to a measuring cylinder, the coloring agent solution is added and the final volume is made up with glycerin. This solution is filtered to remove if any foreign particles or any undissolved substance are present. Three same quantity elixirs with the 3 different concentration of the colorant are used. The amount of colorant added is 0.0034 %, 0.034 % and 0.067 % in 30 ml of F1, F2 and F3 respectively.

Evaluation:

It is very essential to maintain a uniform standard of the medicated formulation. The parameters used to evaluate the formulation are pH, visual inspection, clarity, odour, U.V spectroscopy, and exposing the formulation to different environmental conditions like sunlight, U.V. cabinet and room temperature under shade etc. The formulation is kept for 3 months for evaluation to know the miscibility, compatibility and stability.

Results and Discussion:

After extraction concentrated color was kept aside for further usage. The elixir is prepared by taking the quantities of all ingredients as mentioned in table 1. Three formulations were made using different concentrations of colorant as shown in table 2.

The parameters evaluated are pH of elixir, Visual Inspection under Sunlight, Visual Inspection under U.V. Cabinet, Visual Inspection at Room temperature under shade, Clarity of elixir, odour of elixir, UV Spectroscopy after exposing to sunlight, shade, UV cabinet and all results are shown in tables 3 to 9. It was found that the pH of the formulations, colour and the marketed formulation were observed to be pH 8.57 on average. Under sunlight the colour intensity decreased gradually with the formation of dark ring. Under the

influence of UV cabinet formation of light and dark coloured ring was observed with F2 & F3. At room temperature under shade there was no change in any formulation. The formulation after evaluation under sunlight, UV cabinet and at room temperature under shade, were subjected to UV spectroscopy which shows significant decrease in absorbance in all the three F1 & F2 but no significant decrease is seen in F3, where the color concentration is 0.067%.

Table No. 3: Measurement of pH

Formulation code	Elixir (ml)	Color added	pH measurement
F1	30	0.0034 %	8.65
F2	30	0.034 %	8.75
F3	30	0.067 %	8.87
Annatto color	-	-	8.15
Marketed product	60	-	8.47

Table No.4: Visual Inspection under Sunlight

Formulation code	Elixir (ml)	Color added	Color intensity
F1	30	0.0034 %	Colorless
F2	30	0.034 %	Decrease
F3	30	0.067 %	Decrease with formation of dark color ring

Table No.5: Visual Inspection under U.V. Cabinet

Formulation code	Elixir (ml)	Color added	Color intensity
F1	30	0.0034 %	No change
F2	30	0.034 %	No change but formation of light color ring
F3	30	0.067 %	No change but formation of dark color ring

Table No.6: Visual Inspection at Room temperature under shade

Formulation code	Elixir (ml)	Color added	Color intensity
F1	30	0.0034%	No change
F2	30	0.034%	No change and no formation of colored ring
F3	30	0.067%	No change and no formation of colored ring

Clarity

All the elixir was found clear without any foreign particles after 3 months also.

Odour

No odour in the formulation before and after the evaluation.

Table No.7: UV Spectroscopy after exposing to sunlight

	Sample quantity(ml)	Color added	Before evaluation		After evaluation	
			wavelength	absorbance	wavelength	absorbance
F1	30	0.0034%	453	0.13	453	0.05
F2	30	0.034%	453	2.3	453	0.27
F3	30	0.067%	453	3.4	453	1.13

Table No.8: UV Spectroscopy after exposing to U.V cabinet

	Sample quantity(ml)	Color added	Before evaluation		After evaluation	
			wavelength	absorbance	wavelength	absorbance
F1	30	0.0034%	453	0.13	453	0.21
F2	30	0.034%	453	2.3	453	2.21
F3	30	0.067%	453	3.4	453	3.0

Table No.9: UV Spectroscopy after exposing to Shade

	Sample quantity(ml)	Color added	Before evaluation		After evaluation	
			wavelength	absorbance	wavelength	absorbance
F1	30	0.0034%	453	0.13	453	0.11
F2	30	0.034%	453	2.3	453	1.1
F3	30	0.067%	453	3.4	453	2.21

Comparison with the Marketed Product:

Formulation taken for comparison is a paracetamol pediatric elixir under the brand name PARACEB manufactured by Cipla. The marketed product had the paracetamol concentration of 125 mg for every 5ml, which is the concentration maintained in the formulation of the elixir.

The coloring agent used in the marketed product is Erythrosine, the concentration sufficient to produce pink color.

Table No.10: Comparison with the Marketed Product

Comparison	Marketed product	Prepared formulations (F1, F2 and F3)
Name of the coloring agent.	Erythrosine.	Bixin and Norbixin.
Concentration of the coloring agent.	Quantity sufficient to produce pink color.	F1= 0.0034 % F2= 0.034 % F3= 0.067 %
Concentration of paracetamol.	125 mg of paracetamol in every 5 ml of the elixir.	125 mg of paracetamol in every 5 ml of the elixir.
Origin.	Synthetic.	Natural.
Colour.	Pink.  Fig.14: Color of marketed product.	Yellow, orange and orange red depending on the concentration.  Fig.15: Colors of formulations.
pH	8.47	F1-8.65, F2- 8.75 and F3-8.97.
Avoid exposure to.	High temperatures.	Sunlight and U.V.cabinet

Conclusion

The Annatto coloring agent was found to be compatible with all the ingredients of the formulation and is suitable for use. The evaluation tests performed on the formulation gave a general picture that the Annatto coloring agent is stable and safe when prepared and stored in dark place. The successful preparation and evaluation of this paracetamol elixir directs us towards the usage of natural coloring agents in other dosage forms like emulsion, suspension, tablets etc., and stop depending on synthetic colorants not just make safer preparations at economical prices but to make use of these unnoticed natural agents.

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