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# DESIGN OF SOLID ORAL DOSAGE FORM AND ITS QUALITY CONTROL ASSESSMENT OF URAI MATHIRAI – A TABLET FROM SIDDHA FORMULATION FOR IMMUNO MODULATION IN PEDIATRIC COMMUNITY.

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## ABSTRACT

Urai Mathirai has been use traditionally for the past five decades as an Immunomodulator. The details of preparation and its indications were listed in Hospital Pharmacopeia of Indian medicine. However, there is no uniformity in dosage mentioned and no clinical evidence to support its efficacy. The present study was focused to develop standard operating procedure for the preparation of Uraimathirai at a dose of 50 mg, once daily for six months and to test its efficacy in preventing recurrent respiratory illness. Pre-formulation studies were carried out to rule out the interaction between the formulation and excipients. Three formulations (*viz* F1, F2 & F3) of Uraimathirai 50 mg were developed by wet granulation method using microcrystalline cellulose (diluents), polyvinyl pyrrolidone (binder), and talc (glidant & lubricant). The tablets were evaluated for both pre-compression and post compression parameters. Among three formulations, F3 showed the best results and abide with standards of PLIM guidelines.

**KEYWORDS:** Urai Mathirai, Conventional tablet dosage forms, Wet granulation method, PLIM guidelines.

## 1.0 INTRODUCTION

Diseases of respiratory tract are among the most widely recognized of human infirmities. They are significant reason for expanded dreariness and death rates in youthful youngsters in India. Upper respiratory tract infection is a nonspecific term used to portray intense contaminations including the nose, paranasal sinuses, pharynx, larynx, trachea and bronchi.[1]

Intense respiratory tract diseases cause 4.5 million deaths among school age kids each year, this devastation occur in developing countries. Pneumonia unassociated with measles causes 70 percent of these deaths; post-measles pneumonia, 15 percent; pertussis, 10 percent; and bronchiolitis and croup disorders, 5 percent. Both bacterial and viral pathogens are accountable of these deaths. The most critical bacterial mediators are Streptococcus pneumoniae, Haemophilus influenzae and Staphylococcus aureus. The information on bacterial etiology of pneumonia amid the initial 3 months of life is constraint and no data on the part of chlamydia and pertussis in this age period is accessible. The dispersal of viral pathogens in developing nations can be concise as: respiratory syncytial infection, 15-20 percent; parainfluenza infections, 7-10 percent; and flu A and B infections and adenovirus, 2-4 percent. Mixed viral and bacterial diseases happen much of the time.[2]

Hazard factors that increase the rate and seriousness of upper respiratory disease in developing nations incorporate substantial large family size, lateness in the birth order, crowding, low birth weight, malnutrition, vitamin A deficiency, lack of breast feeding etc. Effective interventions for prevention and medical case management are urgently needed to save the lives of many children predisposed to severe disease.[3]

Siddha system of medicines, being the oldest ancient ways in which of maintaining a healthy life vogue remains rife and emphasizes the importance of physical, emotional, psychological, social well-being. The real strength of Siddha system relies on preventive and encouraging health care deliveries and additional stress is given towards malady interference than management. All over the world drug developers put extra effort to design any drug for pediatric community as it involves stringent procedures such as palatability, less toxicity, non- dependence and non – cumulative. The present study was to overcome the drawbacks of siddha system of medicines like poor patient compliance and improper dosing. Urai Mathirai is a drug used for the past 3 decades in the form of long finger size bullets which are rubbed and administered through breast milk with children's to improve immunity to get free from health hazards such as frequent respiratory infections /gastrointestinal infections and

anorexia. However rubbing of bullets sometimes may differ and proper dose may not be obtained. In order to overcome 50 mg Urai Mathirai was made into conventional tablet form with use of standard modern formulation techniques.

## 2. 0 MATERIALS AND METHODS

Urai Mathirai Preprocess coarse powder, polyvinyl pyrrolidone (sigma), Talc (sigma), all other reagents were obtained from Siddha Central Research Institute, Arumbakkam, Chennai. Micro crystalline cellulose obtained from Signet Chemical Corporation Pvt Ltd. Pre-formulation and post compression parameter testing is an investigation of physical and chemical properties of a drug substance and its formulation. It involves physical characterization, bulk characterization, drug excipient compatibility study, weight variation, thickness, hardness and friability.

### *2.1 PRE FORMULATION PARAMETER STUDY*

#### *2.1.1 Physical Characterization*

*a) Organoleptic properties:* Colour taste and odour of the drug (Urai Mathirai formulation) were evaluated and recorded in a descriptive terminology.

***b)*** *Colour:* A small quantity of formulation was taken in butter paper and viewed in well-illuminated place to confirm its colour.

***c)*** *Taste and odour:* Taste and Odour were recorded.

#### *2.1.2 Bulk Characterization*

Bulk characterization of drug namely bulk density, tapped density, compressibility index and hausners ratio of the drug were evaluated and recorded.

*a) Bulk Density***:** It refers to a measurement to describe packing of particles. Bulk density is used to determine the amount of drug that occupies the volume in mg/mL. It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder in to a measuring cylinder and the initial volume was noted. This initial volume is called bulk volume. From this, the bulk density is calculated according to the formula mentioned below. It is expressed in g/mL and is given by.

$$\text{Bulk density (g/mL)} = \frac{\text{Weight of sample (g)}}{\text{Volume occupied by the sample (mL)}}$$

*b) Tapped Density:* Weighed quantity of drug was taken in a graduated cylinder. Volume occupied by drug was noted down. Then the cylinder was subjected to 500, 750 & 1250 taps in tap density tester According to USP, the blend was subjected for 500 taps. The percentage volume variation was calculated and subjected for additional 750 taps. The percentage variation was calculated and recorded.

$$\text{Tapped bulk density (g/cc)} = \frac{\text{Mass of powder (g)}}{\text{Tapped volume of the powder (cc)}}$$

*c) Compressibility Index:* Weighed amount of drug was transferred to 100ml graduated cylinder and subjected to 500,750 & 1250 taps in tap density tester. The difference between two taps should be less than 2%. The percentage of compressibility index was calculated using formula

$$\text{Compressibility Index (CI)} = \frac{V_i - V_t}{V_i} \times 100$$

Where, $V_t$ = Tapped volume; $V_i$ = Untapped volume

*d) Hausner's ratio:* It provides an indication of the degree of densification which could result from vibration of the feed hopper.

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

*e) Angle of repose:* Angle that can be obtained between the free surface of a powder heap and horizontal plane. The angle of repose was measured by allowing the powders to fall over a graph sheet placed on horizontal surface through a funnel kept at a certain convenient height. The height of the heap was measured and then circumference of the base of heap was drawn on a graph sheet with the help of a pencil. The radius of the circle obtained was measured. The angle of repose is given as,

$$\theta = \tan^{-1}\left(h/r\right)$$

$\theta$ = angle of repose; h = height of the heap; r =radius of the base of the heap

## 2.2 DRUG –EXCIPIENT COMPATIBILITY STUDIES

### *2.2.1 FT- IR Spectroscopy*

The interference by the excipients was evaluated by Bruker ALPHA II FT-IR spectrometer using potassium bromide disc method with spectrum range 400-4000 $cm^{-1}$. The spectra were

obtained for pure drug, excipients, drug with excipient in the concentration of 1:1 ratio and compared.

### *2.2.2 Formulation and Evaluation of Urai Mathirai*

The Urai Mathirai 50mg were prepared by wet granulation method using microcrystalline cellulose (diluents), polyvinyl pyrrolidone (binder), and talc (glidant & lubricant). The active ingredient and diluent were weighed accurately, passed through sieve 40 mesh and mixed thoroughly with help of poly bag for 15mins. Solutions of the binding agent were prepared by adding povidone into water with stirring. The powder mass was wetted with the binding solution until the mass has the consistency of damp. The wet mass was passed through a 20 mesh screen. Collected wet granules was placed on large trays and allowed to drying with use of tray dryer, fluidized bed dryer. After drying, the granulation was reduced in particle size by passing smaller mesh screen 50% of talc was added finally and mixed for 5 mins. The powder blends were evaluated for pre-compression parameters like bulk density, tapped density, angle of repose, compressibility index and hausner's ratio. The blends were compressed into tablets on a 16 station tableting machine and evaluated for post compression parameters. The composition of three formulations were shown in Table 1.

**Table 1: Formulation of Urai Mathirai tablets.**

| Materials | F1 | F2 | F3 |
|---|---|---|---|
| **Urai** | 50 mg | 50mg | 50mg |
| **MCC (112) (%)** | 1.85 | - | - |
| **MCC (102) (%)** | - | 11.67 | 11.67 |
| **PVP k30 (%)** | 5.56 | 4.17 | 4.17 |
| **Talc (%)** | 2.78 | 0.83 | 0.83 |
| **Total** | 54mg | 60 mg | 60mg |

MCC- Microcrystalline cellulose; PVP-Polyvinyl pyrrolidone

## 2.3 POST COMPRESSION PARAMETER STUDY

***2.3.1 Weight Variation test:*** 20 tablets were taken and weighed individually. Average weight was calculated and compared the individual tablet weight to the average weight. The tablet passes the test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

**Table 2: Weight variation limits.**

| S. No. | Average weight of tablet | Percentage |
|---|---|---|
| 1. | 80 gm or less | +/- 10% |
| 2. | More than 80 mg & less than 250 gm | +/- 7.5% |
| 3. | 250 mg or more | +/- 5% |

***2.3.2 Thickness:*** The thickness of formulations was determined using a Vernier Caliper and expressed in the form of millimeter.

***2.3.3 Hardness:*** The hardness of the tablets was checked using the hardness Monsanto Tester and expressed in the form of kilogram per centimeter square.

***2.3.4 Friability:*** In all formulations, tablets were selected randomly and weighed. Tablets were then placed in friability testing apparatus i.e. Roche friabilator and rotated at a speed of 25 rpm for 4 minutes. Tablets were then weighed and a friability value was determined. The difference in weight was noted and expressed as percentage friability of fabricated tablets was noted the Official limits not more than 1%.

$$\% \text{ Friability} = \frac{W_1 - W_2}{W_1} \times 100$$

***2.3.5 Disintegration Test:*** The disintegration apparatus contains 6 glass tubes that are long; open at the top and 10 mesh screen at the bottom end. To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in a 1-L beaker of distilled water, at 37 ± 2° C such that the tablet remain 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement. Move the basket containing the tablets up and down through a distance of 5-6 cm at a frequency of 28 to 32 cycles per minute. Floating of the tablets can be prevented by placing perforated plastic discs on each tablet. According to the test the tablet must disintegrate and all particles must pass through the 10 mesh screen in the time specified. If any residue remains, it must have a soft mass.

## 3.0 RESULTS AND DISCUSSIONS

### 3.1 PRE FORMULATION STUDIES

#### 3.1.1 Organoleptic characters

The organoleptic characters of Urai Mathirai were studied. The study showed that the drug was a deep green colour powder and sour taste with herby odour.

### 3.1.2 Bulk characterization

The bulk density of Urai Mathirai was found to be 0.5383 gm/cc and the tapped density was found to be 0.5897 gm/cc. The results indicated that the values were similar to the specific standard. The angle of repose was did as per the procedure and the value was found to be 30º 19'. The final lubricated blend (F3) had good flow property. The results were shown in the Table 3.

**Table 3: Bulk characterization of lubricated blends of optimized formulation (F3).**

| Parameters | Results | Reference value | Flow property |
|---|---|---|---|
| **Bulk density (gm/cc)** | 0.5383 | - | - |
| **Tapped density (gm/cc)** | 0.5897 | - | - |
| **Compressibility index (%)** | 9.548 | ≤10 | Excellent |
| **Hausner's ratio** | 1.095 | 1.00–1.11 | Excellent |
| **Angle of Repose (θ)** | 28° 2' | 20-30 | Good |

### 3.2.1 Drug - Excipients compatibility study

The FT-IR spectra of the Urai Mathirai pure drug and physical mixture of drug– excipients were recorded using FTIR spectrophotometer in order to check interaction between drug and excipients. The characteristic peaks due to pure Urai Mathirai had appeared in the spectra without any markable change in the position in the spectra of drug-excipients. The results indicated that there was no chemical interaction between Urai Mathirai drug and excipients and suitability of the excipients in the formulation. The results were shown in the (Fig.1 and Table 4).

**Table 4: The Drug and Excipients compatibility studies.**

| Excipients | Compatible | Incompatibile |
|---|---|---|
| Urai+ Microcrystaline cellulose | √ | - |
| Urai+ Polyvinyl pyrollidone | √ | - |
| Urai+Talc | √ | -- |
| Lubricated blend (F3) | √ | - |

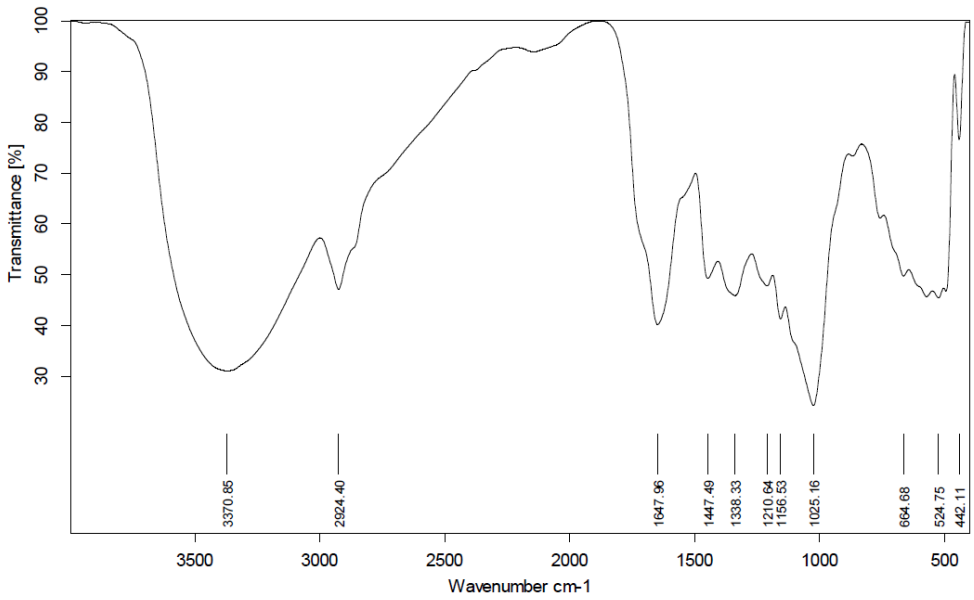


**Fig 1: Stack plot of FT-IR spectrum F3.**

### 2.2 Post compression parameters

The optimized formulations of Urai Mathirai (F3) was evaluated for post compression parameters like the weight variation, thickness, hardness and friability and the values were shown in (Fig.2 and Table 5).

**Table 5: Post compression parameters of optimized formulation (F3).**

| | |
|---|---|
| **Weight variation** | 63 ± 0.71 mg |
| **Hardness** | 3.5 kg/cm$^2$ |
| **Thickness** | 1±0 .08 mm |
| **Disintegration time** | 13 mins ± 0.82 |


**Fig 2: Formulation (F3).**

## 4.0 CONCLUSION

Among three formulation (F3) Urai Mathirai 50mg showed good pre-formulation and post compression parameters which were well within the limits. It will be the promising approach to deliver the drug to treat children's from health hazards such as frequent respiratory infections /gastrointestinal infections and anorexia and also economical for scale up process. This tablets minimize improper drug administration, enhance the therapeutic efficiency and for better patient compliances from previous traditional practice. The study will be extended to *pre-clinical and clinical* evaluation.

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