Effect of *hsei-weik-za* in patients with *Vatarakta* with special reference to gouty arthritis

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Introduction

- The incidence of *Vatarakta* increases rapidly between the ages of 30 and 50 years, and the prevalence then continues to increase with age
- However, in patients over the age of 60, *Vatarakta* affects both men and women equally
- According to the western treatment, the variety of drugs like uricosuric, anti-inflammatory drugs, NSAID, glucocorticoids are used to treat the gouty arthritis symptomatically, which have many potential adverse effects like vomiting, gastro intestinal bleeding, hepato renal toxicity etc.

- Also in Myanmar, Myanmar traditional medicine practitioners have been using *Hsei-Weik-Za* (*HWZ*) for the patients with *Vatarakta* since several years
- According to the traditional medicine in the text of Ayurveda U Tin Oo said that *HWZ* is significantly used for *Vatarakta chikitsa* (treatment) because of their *tridoshahara* (pacified *tridosha*) and *raktashodhaka* (purification of blood) properties

- Hence, the present study aims to evaluate the efficacy of combined effect of Hsi-mee-dauk (*Gloriosa superba* L.), one of the drugs of choice in *Vatarakta* and Taung-ma-yoe (*Alstonia scholaris* L.) quoted to have pain relieving and diuretic activity
- Thus the present study was carried out with a target to flit upon a better efficacious "*Shamana Aushada*" (the drugs are subsidence of diseases and symptoms) for *Vatarakta*

Objectives

General Objective

- To study the effect of *Hsei-Weik-Za* in patients with *Vatarakta* W.S.R. to Gouty Arthritis

Specific Objectives

- To identify the organoleptic properties of *Hsei-Weik-Za*
- To develop formulation of tablet with a view to standardize various formulation parameters
- To evaluate the therapeutic response of *Hsei-Weik-Za* on *Vatarakta* in patients
- To explore the effect of *Hsei-Weik-Za* on uric acid level

Material and Methods

- **Materials**
  - Tuber of *Gloriosa superba* L.
  - Barks of *Alstonia scholaris* L.
  - Sodium chloride
  - Test drug (tablets of *HWZ*)

Methods

Purification of Hsi-Mee-Dauk

- The tuber of *G. superba* was roasted until stopping of fire sparkling so that it can remove poison.

Before purification of the tubers of *G. superba* L.

After purification of the tubers of *G. superba* L.

Before roasting Sodium Chloride

After roasting Sodium Chloride

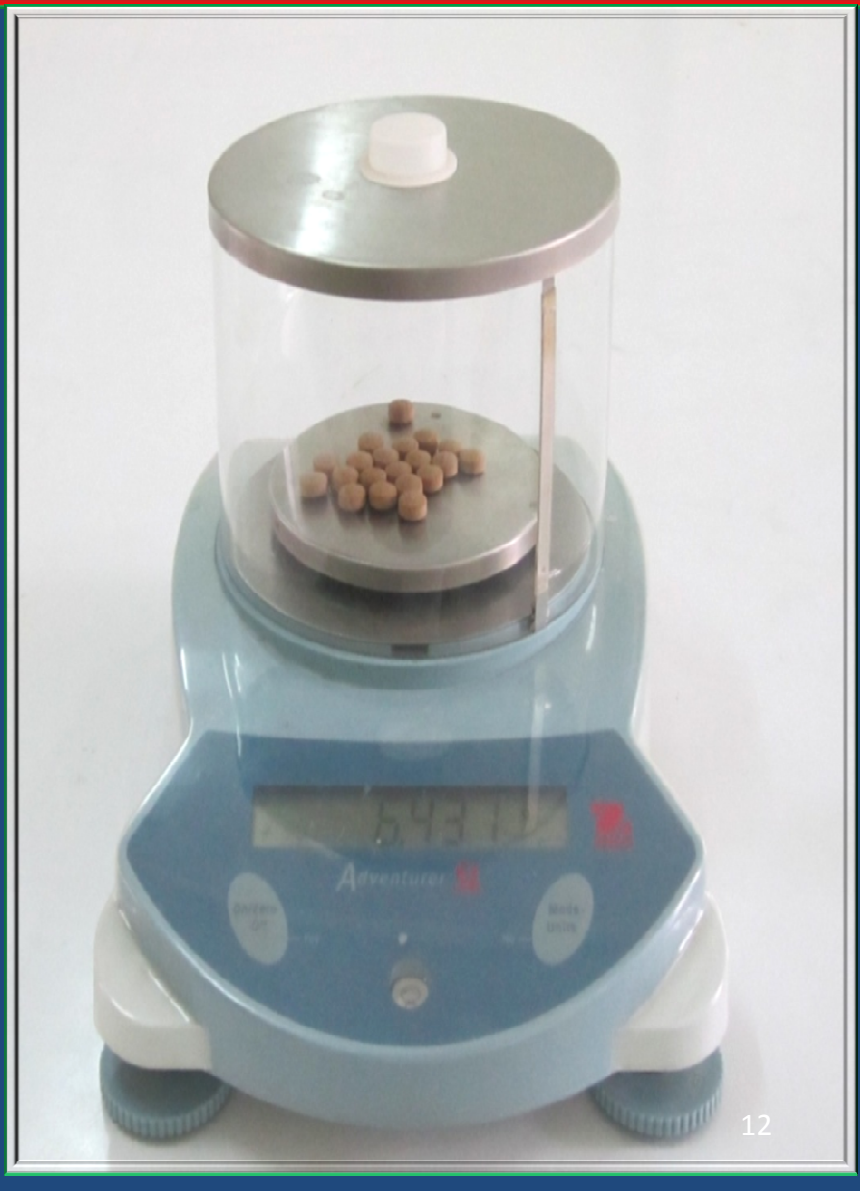
Preparation of *HWZ* Tablets

- Dried barks of *A. scholaris*, purified tubers of *G. superba* and roasted salt were made powder with grinding machine to obtain fine powder of *HWZ*
- *HWZ* powder was prepared as tablet dosage form
- It was unit dosage form in which one usual dosage of the drug has been accurately placed
- Tablets were prepared by wet granulation method

- The tablets were evaluated by measurements of uniformity of weights, friability, hardness, disintegration time, diameter and thickness (British Pharmacopoeia, 2004)

Weight Uniformity Tester

- Twenty tablets were weighed individually using a analytical balance with the precision of 0.05 mg and readability of 0.1 mg, from which the mean was calculated and percentage deviations were determined



Hardness Tester (Crushing strength)

- The crushing strengths of tablets were determined individually with the digital hardness tester (YPD 200C), following 10 tablets were used and the mean crushing strength was calculated

Friability Tester

- The friability of 20 tablets was determined using Roche friabilator (CJY. 300B)

- This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution.
- Pre-weighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions.
- Tablets were dedusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula;

$$F = \frac{\text{Before operation total weight} - \text{After operation total weight}}{\text{Before operation total weight}} \times 100$$

Disintegration Tester

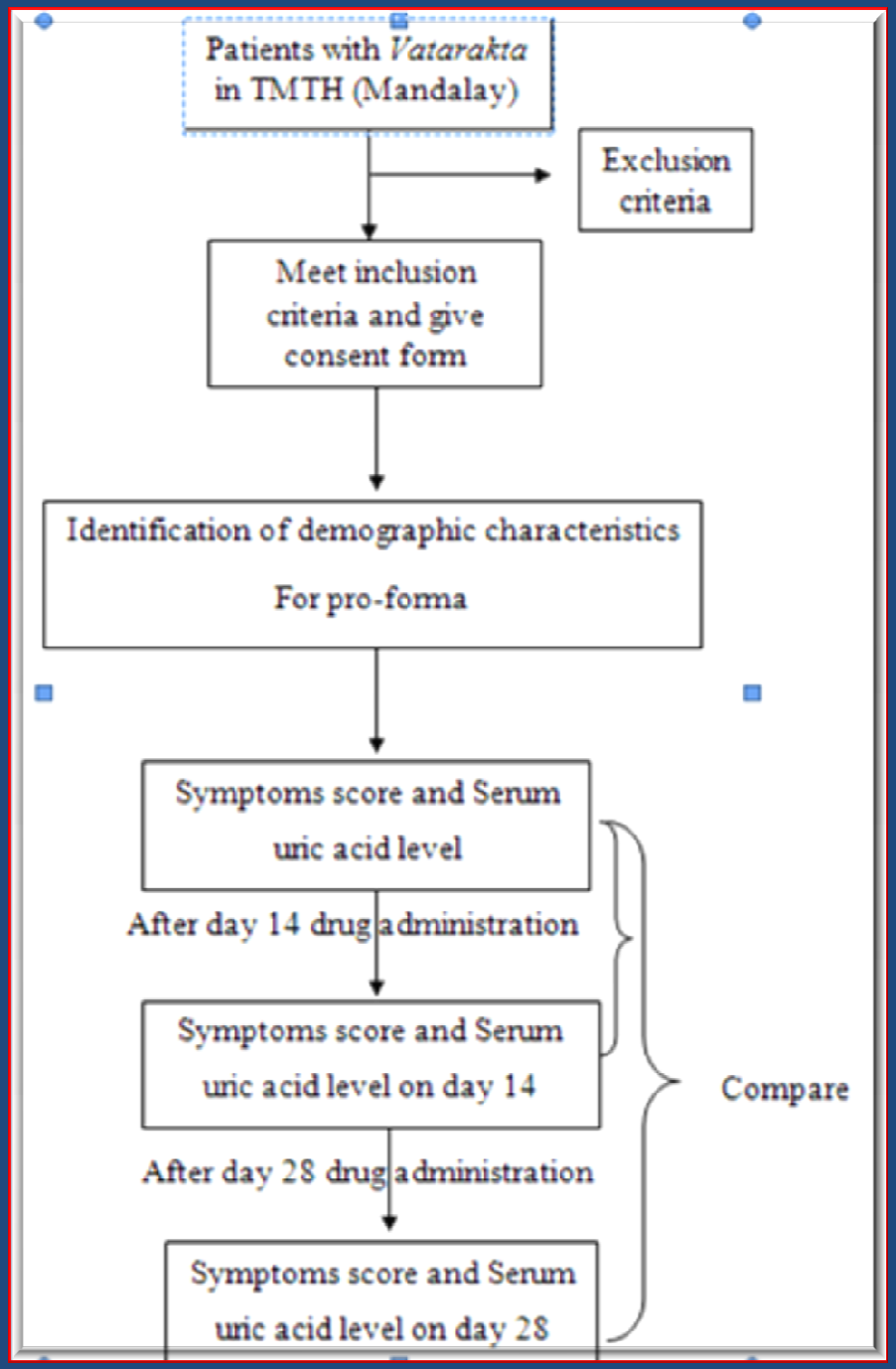
- The disintegration time of tablets was determined using tablet disintegration test apparatus (Senapati bapat marg Japan) according to the method described in the British Pharmacopoeia 2004

- Six tablets were placed in each compartment of the disintegration apparatus, with 180ml water thermostated at as the medium
- The tablets were considered to have passed the test after the 6 tablets passed through the mesh of the apparatus less than in 15 minutes

Medication Procedure

- After taking the consent form, the subjects were measured for base line data including BMI, blood pressure and uric acid levels
- Total experimental period was 28 days, in which each subject was given 2gm (5 tablets) of *HWZ* three times per day
- All subjects were instructed about this study for taking the tablets with warm water after food daily at 8 am, 2 pm and 8pm

Flow chart for study procedure



The tablets of *Hsei-Weik-Za*

- All subjects were given the packet of *HWZ* tablets every 14th day by investigator
- One packet contains 84 gm (210 tablets) of *HWZ*
- Any side effects of the tablets of *HWZ* and changes in concomitant medications were assessed by history taking and physical examination at every visit by investigator

Results

Organoleptic properties of *Hsei-Weik-Za*

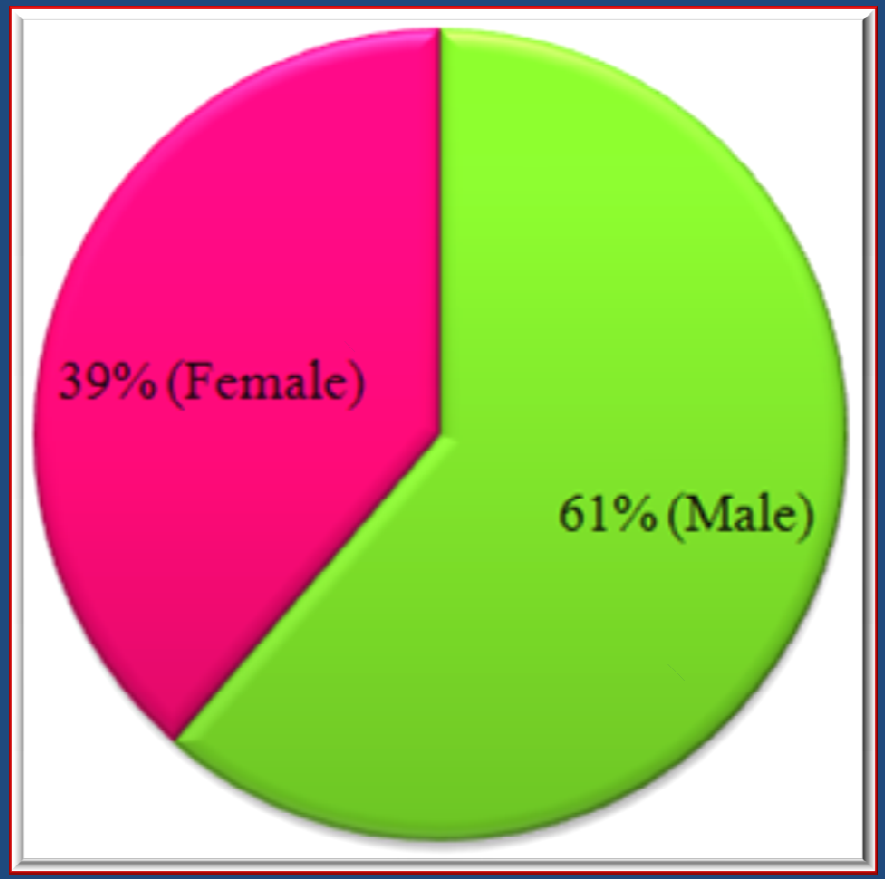
- **Name of drugs** - *Hsei-Weik-Za*
- **Colour** - Brownish white
- **Odour** - Smell of Taung-Ma-Yoe
- **Taste** - Salty and Bitter

Standardization parameters data for *Hsei-Weik-Za* tablets

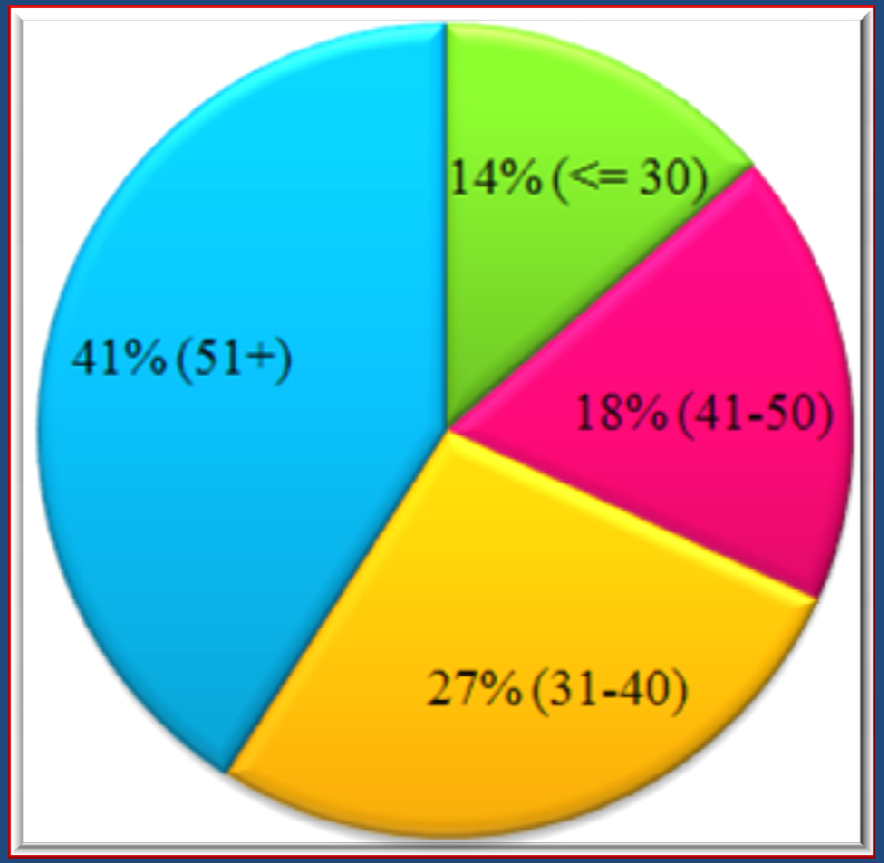
Parameter	Result		
	Batch 1	Batch 2	Batch 3
Weight variation (mg)	320 ±0.02	320 ±0.02	320 ±0.02
Friability (%)	0.47 ±0.06	0.44 ±0.03	0.47 ±0.06
Hardness (kg/cm^2)	2.5 ±0.13	3.5 ±0.20	4.8 ±0.24
Disintegration time (minutes)	4.35 ±0.29	4.46 ±0.31	5.25 ±0.46
Thickness (mm)	2.3	2.3	2.3

All values are expressed as mean ±SD, n=3.

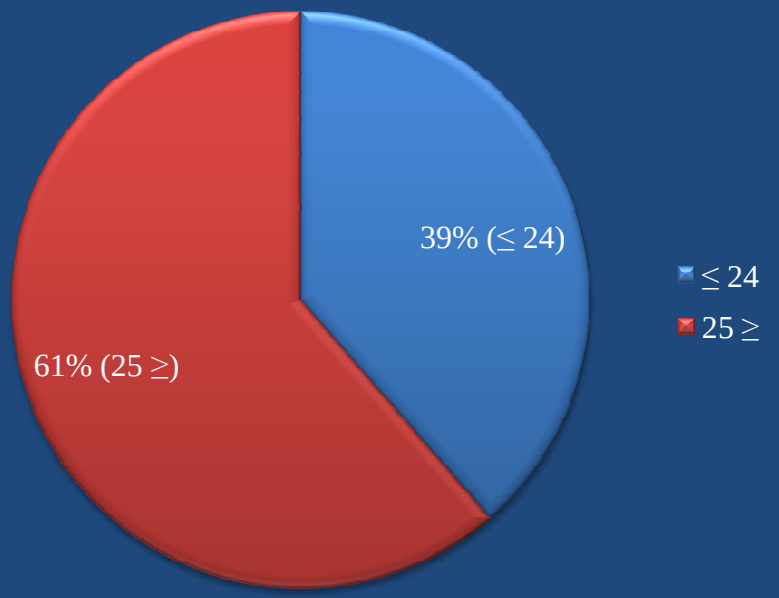
Gender Distribution



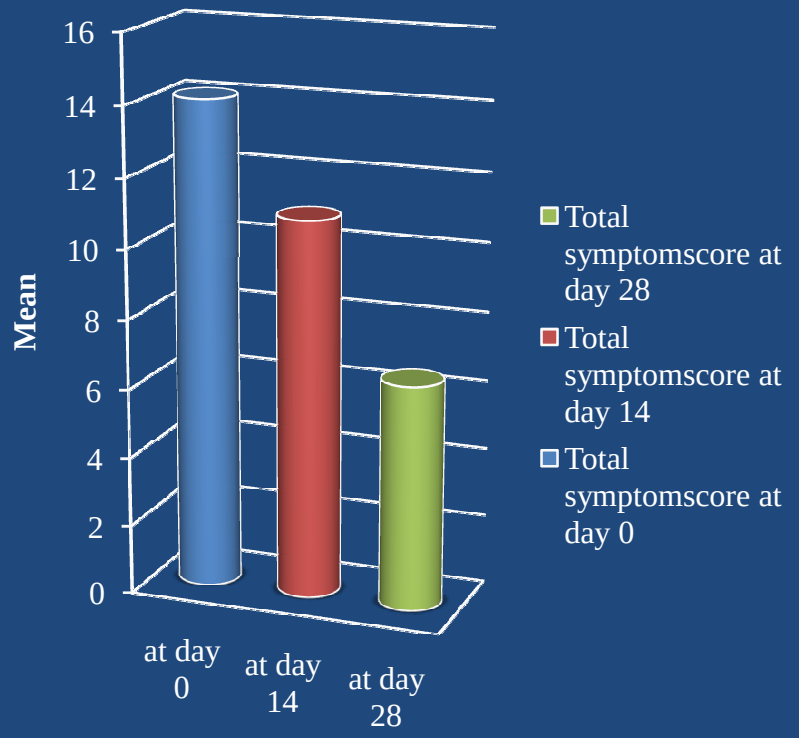
Age Distribution



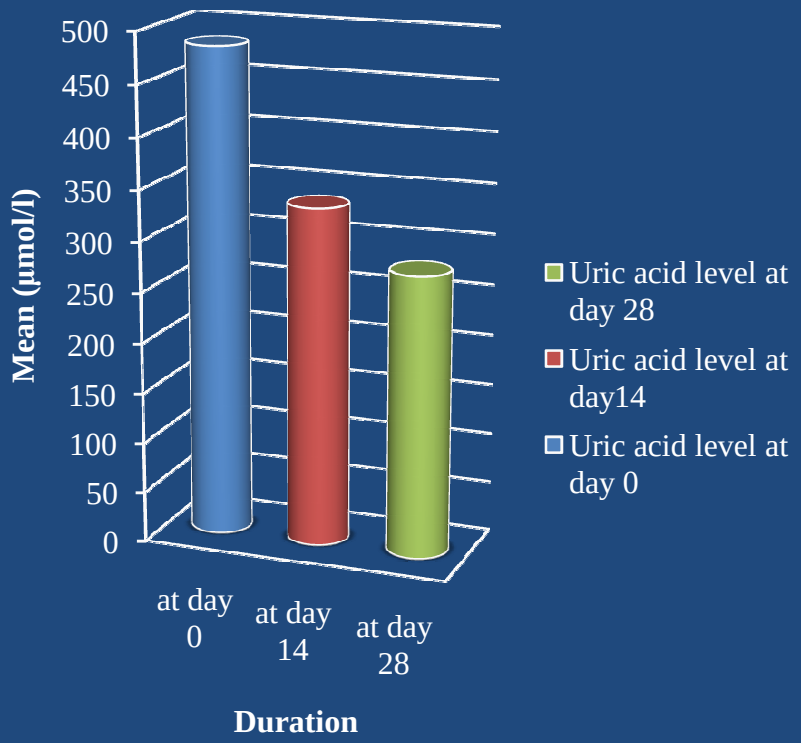
BMI level distribution



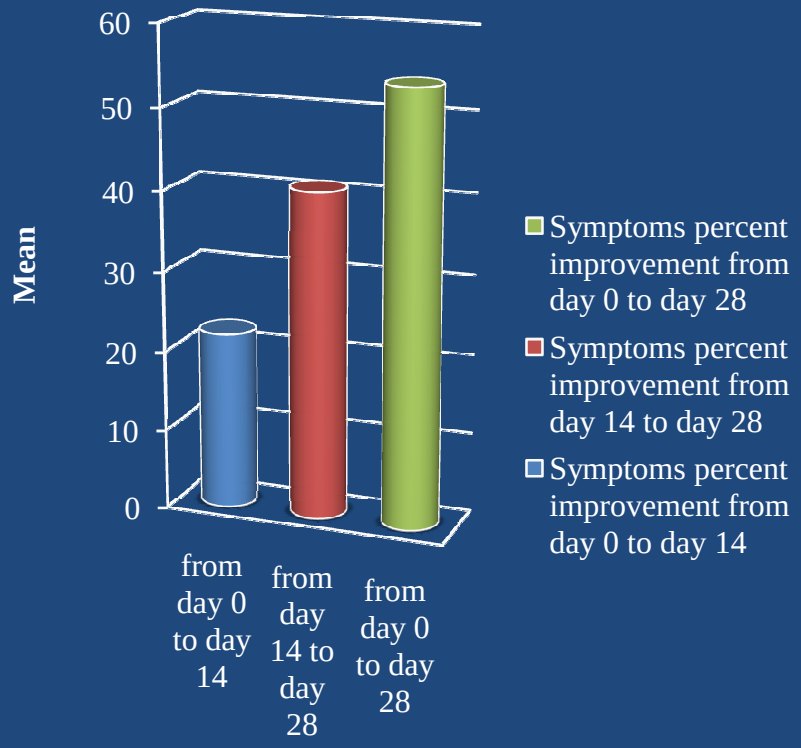
The comparison of mean total symptoms score



The comparison of mean total uric acid level score



The comparison of percent improvement (PI) of symptoms score



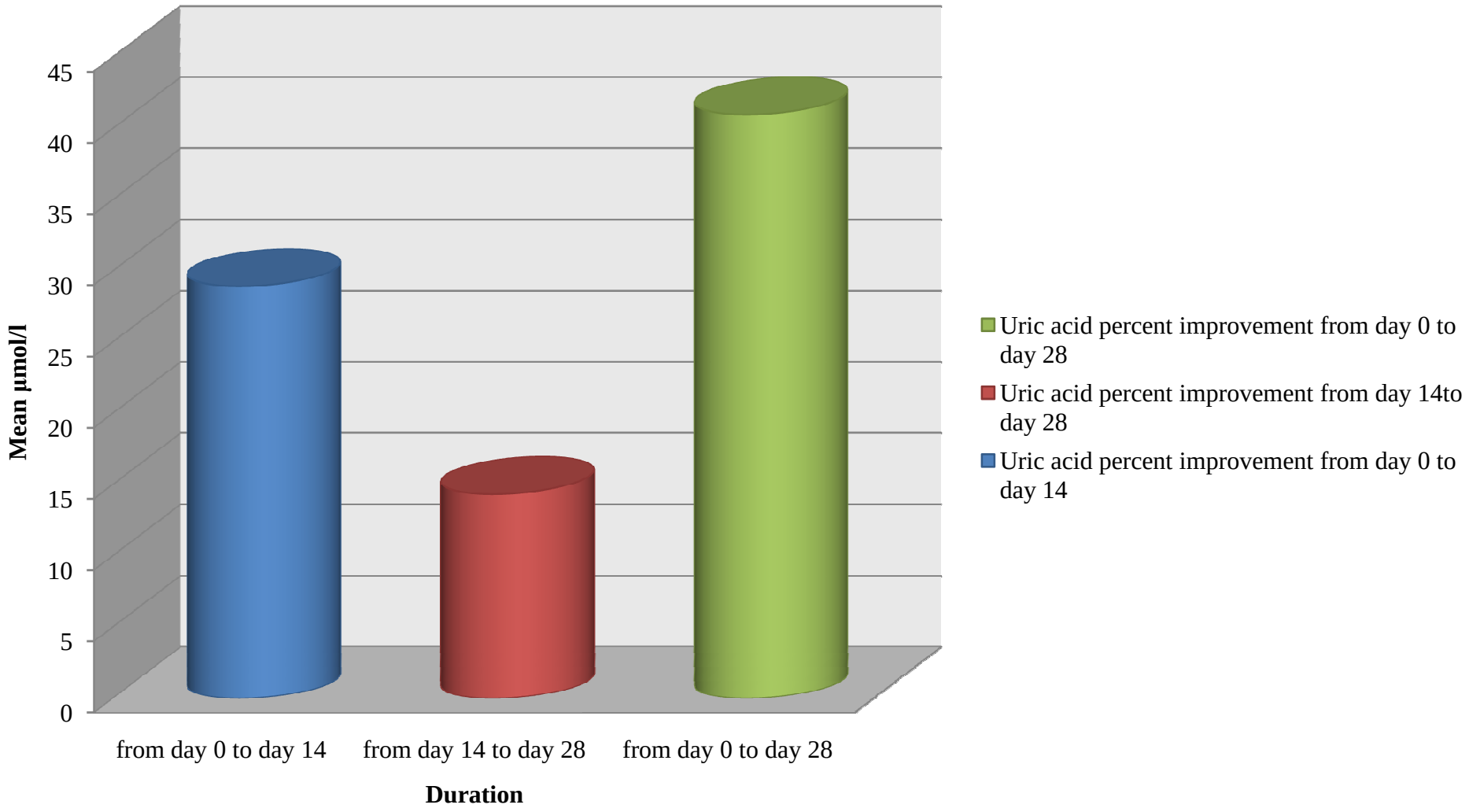
Comparison of percent improvement (PI) of uric acid level score between treatment intervals from day 0 – day 14 to from day 14 – day 28

Comparison of (PI) of symptom score	Paired Differences					t	p value
	Mean	SD	Std. Error Mean	Mean score			
				From day 0 – day 14	From day 14 – day 28		
From day 0 – day 14 to from day 14 – day 28	14.585	41.115	5.288	28.9147	14.3288	2.758	0.008

Comparison of percent improvement (PI) of uric acid level score between treatment intervals from day 0 – day 14 to from day 0 – day 28

Comparison of (PI) of symptom score	Paired Differences					t	p value
	Mean	SD	Std. Error Mean	Mean score			
				From day 0 to day 14	From day 0 to day 28		
From day 0 – day 14 to from day 0 – day 28	-12.067	36.119	2.771	28.9147	40.9823	-4.354	0.000

The comparison of percent improvement (PI) of uric acid level score between treatment intervals



Discussion

- *Vatarakta* is caused by vitiation of *vata* and *rakta* on the joint (*sandi*) where the *silaethaka kapha* is sited
- In clinical practice of traditional medicine, *Vatarakta* is also a common disease according to hospital data
- Totally there were 50 patients registered, of which 44 patients completed the treatment, 6 patients discontinued the treatment

- All the 44 patients registered for the present study were ranging from 25-60 years, of which maximum patients (41%) were between 51-60 years age group, which was followed by (27%) patients in the age group of 31-40 years
- Observation of this study was in accordance with the findings of *Vatarakta* is seen more in aged because the concentration of uric acid increases with the ageing
- In this study, majority of the patients were male (61%) as compared to female patients (39%)

- Textual references also reflect that the predominance of Gouty arthritis in males, this is because the serum uric level rises over twenties men
- According to the organoleptic properties, *Hsei-Weik-Za* has the qualities to relieve both the factors
- The drug having *tikta rasa* (bitter taste) has the ability to give knowledge about inclusion of *ruksha guna*
- On the other hand the drug is attributed the activity it is helpful in excretion of uric acid and helpful in renal calculi

- The hardness of the tablets was within the acceptable range of 4 - 6.5 kg/cm2
- It observed that the hardness increased with increasing binder concentration
- The friability of all the formulations was below 1.0%
- The weight variation of all the formulations were within the range of 320 mg
- Disintegration time of all the formulations are within the official limits of B.P. (2004)
- The disintegration time of tablets was increases with increase in binder concentration

- To compare the signs & symptoms and uric acid levels data before and after treatment, the data were analyzed by paired “t” test
- There were significant statistical changes in week respectively with p value 0.000
- But clinically overall reduction in total symptom was marked improvement with 75% outcome
- Clinically overall reduction in *daha* (hotness or burning sensation) was highly significant with 100% outcome

- Overall response is significantly more in signs & symptoms (marked improvement 75%) when compared to uric acid level from day 0 – day 14 to from day 14 – day 28 (57%) with p = 0.008
- This may be due to the action of *Hsei-Weik-Za* in enhancing the expelling of serum urates through the gut

- It is significant to mention here that as the treatment given by *Hsei-Weik-Za* is found very effective
- These observations suggested that this therapy not only produces symptomatic relief but also control the disease process and may cause long term relief

Conlusion

- *Hsei-Weik-Za* has not toxic effects because of there were not observed any side effects as well as any complaints by the patients during the study period
- According to the results of parameters, *Hsei-Weik-Za* is a very reliable drug for Gouty Arthritis
- Thus *Hsei-Weik-Za* is a reliable oral medicine in the treatment for *Vatarakta*

Suggestion

- Detailed studies should be done to find out standardization and quality control parameters for *Hsei-Weik-Za* should be observed based on following fundamental parameters:

  i. Quality control of crude drugs material, plant preparations and finished products of *Hsei-Weik-Za*.

  ii. Stability assessment and shelf life.

  iii. Safety assessment; documentation of safety based on

  - Acute toxicity test
  - Sub-acute toxicity test
  - Chronic toxicity test

- The study should be conducted in a large sample size.

Acknowledgement

တိုင်းရင်းဆေးပညာဦးစီးဌာနမှ

- ညွှန်ကြားရေးမှူးချုပ်၊ ဒုတိယညွှန်ကြားရေးမှူးချုပ်
- ညွှန်ကြားရေးမှူးနှင့် ဒုတိယညွှန်ကြားရေးမှူးများ၊
- တိုင်းရင်းဆေးတက္ကသိုလ် ပါမောက္ခချုပ်နှင့် တာဝန်ရှိသူ အဆင့်ဆင့်အားလည်းကောင်း၊
- တိုင်းရင်းဆေးဝါးထုတ်လုပ်ရေးစက်ရုံ(မန္တလေး)မှ စက်ရုံမှူး နှင့် ဝန်ထမ်းများ၊

ဆေးသုတေသနဦးစီးဌာန (အထက်မြန်မာပြည်) မှ

- ညွှန်ကြားရေးမှူးချုပ်
- ဒုတိယညွှန်ကြားရေးမှူးချုပ်နှင့် ညွှန်ကြားရေးမှူးများ
- ဆေးဝါးတက္ကသိုလ်၊ မန္တလေးမှ ပါမောက္ခချုပ်၊ ဒုတိယပါမောက္ခချုပ်၊ ကထိကဌာနမှူး နှင့် ဝန်ထမ်းများ
- အဖက်ဖက်မှ ဝိုင်းဝန်း ကူညီပေးကြသူများ အားလုံးကို ကျေးဇူးအထူးတင်ရှိပါကြောင်း

References

- တင်ဦး (ဦး၊ အာယုဗ္ဗေဒ)၊ (၁၉၇၁)၊ ကိုယ်တွေ့အာယုဗ္ဗေဒကုထုံးများ၊ ပထမအုပ်၊ အောင်နိုင်သူပုံနှိပ်တိုက်၊ အမှတ် ၁၁၊ ၁၂၅ လမ်း ကန်တော်ကလေး၊ ရန်ကုန်၊ ၁၆၀–၁၇၃။
- ဟန်ထွန်း (ဦး)၊ (၁၉၉၃)၊ လက်တွေ့အသုံးချဖြန်မှာကုထုံးဆေးပညာကျမ်း၊ ပထမအကြိမ်၊ စိုးမိုးမိတ်ဆက်ပုံနှိပ်တိုက်၊ အမှတ်–၁၄၆၊ ၃၃လမ်း၊ ရန်ကုန်၊ ၁၃၁–၁၃၄။
- Alton, M.E. (1988). Pharmaceutics: The Science of Dosage Form Design. Produced by Churchill Livingstone.
- British Pharmacopoeia (2004). The Several Medical Council Law. The Pharmaceutical Bess. HMSO, London.
- Kulkarni, G.T. and Gowthamarajan, K. Gums and Mucilages, Therapeutic and Pharmaceutical Applications. Natural Product Radiance. assessed 5 June 2002.
- Kopke, A. (2011). The effect of acute gout on inflammatory markers in hyperuricemic patients. M Med Sc University of Pretoria.
- Nwe-Nwe-Win. (2009). Determination of colchine content from dried powder of tuber and seed of *Gloriosa superba* L. locally grown in Myanmar and effect of temperature on colchicines content of tuber. University of Pharmacy, Yangon.
- Shangrow, F. R. (1989). Compressed tablets by Direct Compression. In Licborman, H. A, Lachman, L. and Schwartz, J. B. (Eds). Pharmaceutical Dosage Forms Tablets. Vol (7) (2nd Edition) Marcel Dekker, Inc. U.S.A. 195-245.
- Swe-Swe, Win-Naing, Thein-Zaw-Linn, Khin-Mar-Yi, Sandar-Lin, Swe-Zin-Aung, Min-Zaw-Oo, Tun-Maung, and Kyaw-Zin-Thant. (2013). Traditional Medicine Research Findings (2000-2013), Department of Medical Research (Upper Myanmar), 127.

Thank You