CHAPTER - V

DISCUSSION

&

CONCLUSION
DISSCUSSION

The study titled “Effect of Cakramarda Guggulu Compound in Āmavāta (Rheumatoid arthritis)” is aimed at to prove the efficacy of Cakramarda Guggulu compound in comparison with the Cakramarda seed powder in Āmavāta (Rheumatoid arthritis). The study was designed to investigate the comparative anti-inflammatory activity in albino rats and clinical evaluation of the anti-rheumatoid arthritis activity of both the drugs. The acute toxicity in albino rats and the toleration of the drugs to the patients were also evaluated to confirm about the safety profile of both the drugs.

Before their administration Cakramarda Guggulu compound and Cakramarda seed powder were put to standardization. The microscopic studies were undertaken to evaluate their structural pattern and the quantitative analysis for the purity and strength.

The phytochemical investigation of seeds of Cassia tora (Cakramarda) has been taken for isolation & characterization of mono-methylmono-methoxy dihydroxy-xanthone (Narayan & Rangaswami 1956); emodin, aloe–emodinmonoglucoside (Poethke et.al.1968); amino acids viz. methionine, tryptophan and lysine (Joshi & Nigam 1976 and Niranjan & Katiyar 1979); β sitosterol (Chakrabarty and Chawla 1983); phenolic and related compounds (Choudhary & Choudhary 1987); anthraquinone (Koshioka et.al. 1979); torosachrysone and questin (Kitanaka et.al. 1980); naphtho-pyrone glycosides (Wong et.al. 1989). Thus it appears that the seeds of Cassia tora contain large number of active ingredients, further investigations are required for elucidating the role of these ingredients for their anti-rheumatoid activities.

Thin Layer Chromatography (TLC) study of the trial drugs was performed for scientific standardization. The X-ray analysis of the drug
sample of Cakramarda Guggulu compound showed that the material was polycrystalline in nature and that of Cakramarda seed powder showed that it was amorphous in nature.

The rasa of the trial drugs samples was determined with the help of five volunteers, which verified the Kaṭu rasa in both the drug samples. For the evaluation of Āyurvedic organoleptic standard, the taste threshold of the trial drugs was determined in distilled water, in fresh decoctions of the drugs, decoctions made six hours before, in 1% saline solution and in 1% glucose solution which showed higher values of the taste threshold. This experiment measured the quality of the trial drugs on Āyurvedic parameters (Dhyani, 1978).

The results of the study indicate that along with the anti-inflammatory activity, the Cakramarda Guggulu compound has more significant anti-rhumatoid arthritis activity in Āmavāta (Rheumatoid Arthritis) than Cakramarda seed powder. To communicate this more clearly, the discussion focuses on the animal experiments and the clinical study.

**Animal experiments**

Acute toxicity studies of the trial drug samples on Swiss albino mice (HA strain) showed that both of the drug samples were having no toxic effects and were safe upto a daily dose of 3gm/kg. LD\(_{50}\) of the trial drug samples was proved to be very high.

Animal experiment to evaluate the anti-inflammatory effect of Cakramarda Guggulu compound and Cassia tora (95% alcoholic extracts) on Carrageenan induced rat paw oedema were conducted on albino rats of wistar strain of either sex in 4 groups of 6 animals / group. The observation indicated that in carrageenan rat paw edema (acute model of inflammation),
extracts of both the drugs showed dose dependant activity anti-inflammatory activity. Both of the extracts showed significant anti-inflammatory activity at the dose of 400 mg/kg and 800 mg/kg. The inhibition of 45.23 % after 3 hrs and 23.26 % after 24 hrs (extract of Cakramarda seed powder) was comparable with Piroxicam 3 mg/kg, which showed inhibition of 42.68 % after 3 hrs and 66.38 % after 24 hrs. The inhibition of 47.47 % after 3 hrs and 153.07 % after 24 hrs (extract of Cakramarda Guggulu Compound) was comparable with Piroxicam 3 mg/kg which showed inhibition of 42.68 % after 3 hrs and 66.38 % after 24 hrs. The results of the present study indicate that the combination of Cassia tora and commiphora mukul had additive effect as compared to that of Cassia tora. The other doses did not exhibit significant anti-inflammatory activity. In comparison with Piroxicam, Cassia tora seed powder and the combined extract of Cassia tora and Commiphora mukul were 133 times less potent on weight basis. The finding in the present investigations should be extended to the chronic model of inflammation and other cox-specific assays should be performed.

The animals were observed for any signs of toxicity upon administration of alcoholic extract of Cassia tora and alcoholic extracts of Cassia tora and Commiphora mukul. The animals did not show any abnormal behaviour. There were no deaths recorded during the experimental work. Thus it can be said that these extracts did not show any toxicity at the doses used.

In the view of the observations made in the present work and on the basis of folk-lore claim, it can be said that alcoholic extracts of Cassia tora and Cassia tora plus Commiphora mukul are safe anti-inflammatory agents. The extracts showed a longer duration of actions as there was little difference between the inhibition of oedema at 3hrs and 24hrs which could make the dosing schedule easier.
Clinical study

Under the clinical study total 114 patients were studied of which 58 patients were in group-I (C.G. Compound) and 56 patients were in group-II (Cakramarda seed powder). The revised criteria of the American College of Rheumatology (1987) was adopted for the selection of the patients along with the Ayurvedic symptomatology of the disease was also taken into consideration. A score system was employed for the gradation of different symptoms of the disease and for the assessment of the results.

The observations showed that major number of patients under the study were females in both the groups. Out of total 114 patients, 92 (80.70%) were females, which out numbers the epidemiological data regarding the three times more incidences of this disease in females. The observation of the patients under the study showed that the maximum incidence of the disease was in the 4th and 5th decades, which coincides with the epidemiological data of the disease. (Peter E. Lipsky, 2001).

The maximum patients under the study were the house wives from the middle socio-economic status of the society, which indicates more irregular āhara and vihāra in this group because of the neglected attitude of the society towards them.

Dietary differences in the patients under study were not very prominent. There was only a marginal difference in the incidence of the disease in vegetarians and non-vegetarians because the non-vegetarians are having mixed type of food habits.

Stress appears to be a contributory factor in the causation as well as in complicating the disease process in more than half of the patients under the
study as the proper metabolism is always dependant on the normal state of mind.

The complaint of constipation and passing of loose stools in some of the patients under the study indicate the state of mandāgni and production of āma in them.

The complaint of sleeplessness because of pain and discomfort as reported by a major number of the patients at the time of their admission under the study, shows the intensity of pain and agony which a sufferer of Āmavāta experiences.

The addiction of smoking as indicated (Wolfe Frederick, 2001) could be considered as an important triggering factor of the disease but owing to a very thin number of patients under the study who were smokers, this observation can not be co-related. The over-all addictions were noticed to be much less in the patients under the study.

The predominance of vāta-kaphaja and kapha-pittaja types of śarīra prakṛti (physical constitution) in the patients under the study signifies the prominence of kapha doṣa, hence the drug possessing katu, laghu and ūṣṇa attributes can be of value in the treatment.

Maximum of the patients under study were having rājasa-tāmaṣa type of mānasa prakṛti (mental constitution). This finding is in accordance with the concept that satva is directed towards health and both raja and tama (= stress) are detrimental to the normal immune response.

The predominance of medo sāra in the patients under the study, however indicates the superlative quality of their medo dhāta but also their tendency towards sthūlya (obesity). The excessive kapha āhāra and sedentary habits may have caused agnimāndhya and thus āma formation
which can be considered as the predisposing factor of the disease in these patients.

Involvement of rasavaha and annavaha srotasa in maximum number of patients under the study is in accordance with the samprāptī (aetio-pathogenesis) of the disease as per the Āyurvedic concept.

The average height and correspondingly more weight of the patients under study indicate that on the average patients were over weight, the factor responsible for increasing the tissue injury in the weight bearing joints.

The results of the clinical study in the patients studied under both the groups indicate statistically highly significant (p<0.001) effects of both of the trial drugs on maximum of the cardinal symptoms of the disease.

Most of the major symptoms of the disease like swelling of the joints, tenderness, pain of joints on motion and rest, morning stiffness and fever are the conditions caused in chain sequence by the production and accumulation of āma and the vitiation of vāta doṣa. The significant relief in these symptoms in the patients under both the groups of study indicates the āma pācana and vāta alleviator actions of the trial drugs and thus removal of the restriction of joint movement and increase in the muscle power.

The effect of both of the treatment schedules on morning stiffness can be attributed to their laghu, uṣṇa properties which in turn produce anti-inflammatory and vāta-regulating effects.

Statistically highly significant (p<0.001) effect of both of the trial drugs on swelling can be correlated with their āma-viṣahara, pācana, and kaphaghna actions.
The extant of relief in the symptoms of pain on rest and pain on motion in the patients studied under both of the groups verifies the analgesic effect of Cakramarda. The combination of guggulu with Cakramarda does not look to be having an extra effect in the relief of these symptoms.

Loss of appetite, anorexia, constipation and loose motion are the symptoms pertaining to the mal-functioning of the jatharāgni. Statistically highly significant (p<0.001) relief in these complaints in the patients studied under both the groups, indicate the toning action of both the drugs on jatharāgni.

The increase in the haemoglobin level in both the groups indicates the āma-visahara and pācaka properties of both the drugs, which resulted in the production of the good quality of the rasa and rakta dhātus.

Mean reduction in ESR in the patients studied under both of the groups indicates the reduction in the inflammatory process, improvement in the metabolism and modification in the disease process. These effects of the drugs may be because of their āma-pācana and sroto-śodhana properties.

16 out of 28 sero-positive patients under group–I and 9 out of 16 sero-positive patients under group–II, turned sero-negative after the course of the therapies which shows the immuno-modulatory effects of the trial drugs. This finding is a real indication of the reversal of the disease process and this effect was more significant in the patients studied under group–I with Cakramarda Guggulu compound.

The changes in disease activity were measured through a global assessment on the basis of observations made by both the subject and the physician. The results of the study validate the effects of both the drugs on all the aspects required for the management of Āmavāta (Rheumatoid
Arthritis). But the patients studied under group–I with Cakramarda Guggulu compound showed comparatively better response as out of total 58 patients, 29 (50%) patients have shown good response and 17 (29.31%) patients have shown fair response while out of total 56 patients studied under group–II with Cakramarda seed powder, 21 (35.5%) patients have shown good response and 24 (42.86%) patients have shown fair response.

If taken together, the sum total of the percentages of good and fair response in the patients studied under both the groups are almost the same. Although, the overall effect of Cakramarda Guggulu compound proves to be better but Cakramarda seeds powder as a single drug also proved its worth in the management of Āmavāta (Rheumatoid Arthritis).

No undesired effect of both the drugs has been noticed during the periodical observations of the patients and was not reported by any of the patient studied under both the groups which proves the safety profile of both the drugs.

Since, the classification of the results of the study is based upon relief in the presenting signs and symptoms of the disease and the normalacy in the lab. investigations, these results indicate the effects of the trial drugs on samprāpti vighāṭhāna (breaking of pathogenesis) of the disease in the chain sequence. The increase in jatharāgni, āmaviṣa pācana and  двигателana along with alleviation of increased vāta were the possible pharmacological actions of the trial drugs, which can be inferred from the symptomatic relief and normalacy in the lab. investigations and increase in the functional status of the patients studied and can be interpreted as that the trial drugs are on the one hand are having anti-inflammatory and analgesic actions and on the other hand disease modifying action.
Comparatively, better results in the patients studied under group–I with Cakramarda Guggulu Compound, indicate that the anti-arthritic action of Cakramarda seed powder as validated from the study is more potentiated in combination with Guggulu which in addition to its anti-arthritic action is yogavāhī (a compound that carries the other substances mixed with it, to deep in to the tissues) and rasāyana (adaptogenic). The possible pharmacological actions of Cakramarda Guggulu compound in Āmavāta (Rheumatoid Arthritis) are shown in the flow chart (V.1).
Cakramarda (Cassia tora)  
- Viṣahara
  - Agnivardhaka
  - Kaphahara
  - Srotosodhaka
  - Vātahara
  - Šothahara

Guggulu (Commiphora mukul)  
- Sūkṣma
- Sara
- Rasāyana

Cakramarda mixed with it, to deep into the tissues

Purifies the body from poisonous effects of Āma viṣa

Synergistic action of both the drugs in combination to break the chain of the pathogenesis of the disease Amavāta by
- Jatḥārāgni & Dhatu Agnivṛddhi
- Āma pācana & Kleda śoṣana
- Sroto śodhana
- Vāta śamanam
- Šothaharanā

Carried the drug

Being Rasāyana acts as adaptogenic

There by creating atmosphere in the body for Immuno-adoptability

- Relief in the symptoms of the disease
- Normalacy in lab investigations
- Increase in muscle power and functional status of joints
- Normal metabolism
- Increased immuno-competence

Fig. V.1: Flow chart showing possible pharmacological action of Cakramarda Guggulu Compound in the patients studied under clinical trial.
By virtue of viṣa-hara property, Cakramarda purifies body from the poisonous effects of āmavīṣa thereby creating the atmosphere in the system for immuno-adoptability. Whereas the Guggulu helps in the bio-availability of Cakramarda to the target sites by virtue of its sūkṣma and sara properties and acts as adoptogenic being rasāyana. Uṣṇa, kaphahara, vātahara and śothahara, the common properties possessed both by Cakramarda and Guggulu showed synergistic action in combination to breakdown the chain of the pathogenesis of the disease Āmavāta (Rheumatoid Arthritis). And in sequence there is increase in jatharāgni & dhātuagni which results in āmapācana & kleda-śoṣana followed by srotosodhana, hence, vāta-samana and śothaharana.

This whole equation results into relief in the symptoms of the disease, normalcy in lab investigations, Increase in the functional status of joints, normal metabolism and Increased immuno-competence.

Further studies

1. As the seeds of cakramarda (Cassia tora) contain large number of active ingredients, further investigations are required for elucidating the role of these ingredients for their anti-inflammatory and anti-rheumatoid activities.

2. The finding in the present investigations in rats in acute model of inflammation could be extended to the chronic model of inflammation and other cox-specific assays can be performed.

3. Propagation of rheumatoid arthritis is considered as an immunologically mediated event, the results of the study may be further extended to study the effects of the drugs on this aspect.
4. The long-term clinical studies along with regular follow-up may be of immense value to evaluate the extent of disease modifying effect of trial drugs in this disease of remission and exacerbation.

5. In-door clinical studies on controlled āhāra (diet) and vihāra (routines) can be of more value for implication of strict treatment schedule and nidāna parivarjana (avoidance of aetiological factors).
CONCLUSION

On the basis of the data of present clinical study, animal experiments and the inference drawn about the action of the drugs as discussed, the following conclusions are drawn:

- The Combination of Cakramarda (Cassia tora) and Guggulu (Commiphora mukul) i.e. Cakramarda Guggulu compound is a well tolerated drug and along with the anti-inflammatory activity, it has more significant anti-rhumatoid arthritis activity in Amavāta (Rheumatoid Arthritis) in comparison with Cakramarda seed powder.

- Cakramarda seed powder is also a safe drug devoid of any toxic effects and having significant anti-inflammatory and anti-rhumatoid arthritis activities and can be utilized successfully in Amavāta (Rheumatoid Arthritis).

Hence, the present study testifies the folk-lore claim of the use of Cakramarda in Amavāta (Rheumatoid Arthritis) and this abundantly available drug which is like an unsung song of the nature can be put to judicious use in Amavāta (Rheumatoid Arthritis) in combination with Guggulu for additive effects.