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Comparative Evaluation Of Anti-Inflammatory And Analgesic Activity Of Some Medicinal Plants

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Abstract

Pain And Inflammation Are Disabling Accompaniments Of Many Medical Conditions. So, Controlling Both Pain And Inflammation Assumes The Top Priority For The Physician. Inflammation Is A Part Of A Complex Biological Response Of Vascular Tissues To Harmful Stimuli Such As Pathogens, Chemicals Or Irritants. Therapy Of Pain And Inflammation Has Always Been Debatable. Methods: Rats Were Divided Into 10 Groups Of 6 Animals Of Each. The Antiinflammatory Activity Was Studied With Carrageenan Induced Rat Paw Edema Models. The Analgesic Activity Was Evaluated Using Tail Flick And Eddy's Hot Plate Model. The Ethanolic Extract Of *Balanitesa Egyptiaca* Whole Plant Preparations Were Compared With Indomethacine In Both Acute And Sub Acute Inflammatory Models. The As 400 Mg/Kg Show Significant Increase In Latency To Tail Flick And Eddy's Hot Plate Method Compared To Control Group ($P > 0.05$). The Highest Nociception Inhibition Of Stimulus By As 400 Mg/Kg (400 Mg/Kg) Was Observed Up To 180 Minutes. Various Test Result Parameters Were Statistically Analysed At P Value. The Present Results Suggest That Ethanolic Extract Of *Balanitesa Egyptiaca* Suppresses The First Phase Of Carrageenan-Induced Paw Edema, Thus, Confirming An Nsaid-Like Property.

Key Words: Carrageenan; Indomethacine; Eddy's Hot Plate; Tail Flick Method; Nsaid.

1. Introduction

Plants Have Formed The Basis Of Sophisticated Traditional Medicine Systems That Have Been In Existence For Thousands Of Years And Continue To Provide Mankind With New Remedies. Natural Products And Their Derivatives Represent More Than 50 % Of All The Drugs In Clinical Use In The World. The Principles Of Ayurvedic Medicine And The Medicinal Uses Of Plants Are Contained In Thousands Of Poetic Hymns In The Rig Veda. It Is A Fact That The Village People And Tribes Are Generally Rely On The Medicine Developed From The Plants Directly Or Indirectly. The Who Has Estimated Eighty Per Cent Of The Global Population Relying Chiefly On Traditional Medicine [1]. . In The Beginning Of 21st Century The Phytomedicines Achieved The Reliability To Rescue The Patients From The Fatal Diseases.

Herbal Medicines Have Many Advantages: Have No Side Effects, Better Patient's Tolerance And Relatively Less Expensive. The Chemical Compounds Of Allopathic Medicines Are Costly And Have Side Effects. The Patients Are Seeking The Alternative System Of Medicines Which Are Less Expensive And Will Have No Side Effects. Research On Medicinal Plants Is An Important Fact Of Biochemical Research [2] In India Because Of Several Reasons. Inflammation Is A Disorder Involving Localized Increases In The Number Of Leukocytes And A Variety Of Complex Mediator Molecules. Prostaglandins Are Ubiquitous Substances That Indicate And Modulate Cell And Tissue Responses Involved In Inflammation. The Research Into Plants With Alleged Folkloric Use As Pain Relievers, Anti-Inflammatory Agents, Should Therefore Be Viewed As A Fruitful And Logical Research Strategy In The Search For New Analgesic And Anti-Inflammatory Drugs [3]. Because Excisting Synthetic Molecule Like Non-Steroidal Anti-Inflammatory Drugs (Nsaids) And Selective Cox-2 Inhibitors That Increase The Incidence Of Adverse Cardiovascular Thrombotic Effects [4]. So, In Order To Overcome, There Is Need To Focus On The Scientific Exploration Of Herbal Drugs Having Fewer Side Effects. . Despite The Progress Made In Medical Research During The Past Decades, The Treatment Of Many Serious Diseases Is Still Problematic. Chronic Inflammatory Diseases Remain One Of The World's Major Health Problems [5-7]. Inflammation Is The Response Of Living Tissues To Injury. It Involves A Complex Array Of Enzyme Activation, Mediator Release And Extravasations Of Fluid, Cell Migration, Tissue Breakdown And Repair [8-9]. Inflammation Has Become The Focus Of Global Scientific Research Because Of Its Implication In Virtually All Human And Animal Diseases. The Conventional Drugs Used To Ameliorate This Phenomenon Are Either Too Expensive Or Toxic And Not Commonly Available To The Rural Folks That Constitute The Major Populace Of The World [10-12].

Inflammation Is Considered As A Primary Physiologic Defense Mechanism That Helps Body To Protect Itself Against Infection, Burn, Toxic Chemicals, Allergens Or Other Noxious Stimuli. An Uncontrolled And Persistent Inflammation May Act As An Etiologic Factor For Many Of These Chronic Illnesses [13]. Although It Is A Defense Mechanism, The Complex Events And Mediators Involved The Inflammatory Reaction Can Induce, Maintain Or Aggravate Many Diseases [14]. Currently Used Anti-Inflammatory Drugs Are Associated With Some Severe Side Effects. Therefore, The Development Of Potent Anti-Inflammatory Drugs With Fewer Side Effects Is Necessary.

Material & Method

Selection And Collection Of Plant Material

Plants Were Searched In Madhya Pradesh Particularly Areas Near To Indore. All Plants Were Collected From Area Near Indore. Plants Were Collected As Whole And Herbarium Was Also Prepared And Submitted. Plant Was Authenticated By Dr. Zia Ul Hasan, Botanist, Department Of Botany, Safia College Of Science, Bhopa (M.P.) [Voucher No. *Argyreia Speciosa, Balanitesa Egyptiaca, Gloriosa Superb, Tagetes Erecta* & *Cyathocline Purpurea* 318/Bot/Safia/18, 319/Bot/Safia/18, 320/Bot/Safia/18, 321/Bot/Safia/18, 322/Bot/Safia/18].

Plant Materials Was Washed And Dried Under Shade. Dried Plant Material Was Grinded Using Electric Grinder At Department Of Pharmacy, Dr. A.P.J. Abdul Kalam University, Indore, M.P. Dried Plant Material Was Kept In Closed Air Tight Container Till Any Further Use.

3.2 Crude Extract Preparation

In Present Study, Plant Materials Were Extracted By Continuous Hot Percolation Method Using Soxhlet Apparatus (Kokate, 1994). Powdered Material Of *Argyreia Speciosa, Balanitesa Egyptiaca, Gloriosa Superb, Tagetes Erecta & Cyathocline Purpurea* Was Placed In Thimble Of Soxhlet Apparatus. Soxlation Was Performed At 60°C Using Petroleum Ether As Non Polar Solvent. Exhausted Plant Material (Marc) Was Dried And Afterward Re-Extracted With Ethyl Acetate And Methanol Solvent. For Each Solvent, Soxhlation Was Continued Till No Visual Colour Change Was Observed In Siphon Tube And Completion Of Extraction Was Confirmed By Absence Of Any Residual Solvent, When Evaporated. Obtained Extracts Was Evaporated Using Rotary Vacuum Evaporator (Buchi Type) At 40°C. Dried Extract Was Weighed And Percentage Yield For Each Extract Was Determined Using Formula:

$$\%\ \text{Yield} = \frac{\text{Weight of extract}}{\text{Weight of Plant Material used}} \times 100$$

Prepared Extracts Were Observed For Organoleptic Characters (Percentage Yield, Colour And Odour) And Were Packed In Air Tight Container And Labelled Till Further Use (The Ayurvedic Pharmacopoeia Of India).

3.3 Screening Of Phytochemical Constituents

Qualitative Phytochemical Testing Of Extracts Was Done To Study The Presence Or Absence Of Various Phytochemical Constituents Using Standard Tests [15].

***In-Vivo* Studies**

Table 1: Acute Toxicity Study (According To Oced 423)

Iaec Approval	All Animal Experiments Were Approved By Institutional Animal Ethics Committee (Iaec) Of Pinnacle Biomedical Research Institute (Pbri) Bhopal
Animal Used	*Albino Wistar* Rat
Weight	150 To 200 Gm
Age At The Start Of Study	8-10 Weeks
No. Of Animals/Dose Level	Three (03)
Acclimatization	One Week Prior To Dosing
Identification Of Animals	By Cage Number And Marking On Animal

Diet	Standard Pellets Supplied By Golden Feeds, New Delhi
Water	Purified Water *Ad Libitum*
Sex	Male
Route Of Administration	P.O.
Housing Condition	Animals Were Housed In Separate Cages Under Controlled Conditions Of Temperature (22 ± 2°C). All Animals Were Given Standard Diet (Golden Feed, New Delhi) And Water Regularly.

Table 2: Grouping Of Animals

Plant Used	Group No.	Animals	Sex	Treatment	Dose (Mg/Kg Body Weight)
Argyreia Speciosa	As-I	Aw Rat	Male	Test Group	5 Mg/Kg
	As-Ii	Aw Rat	Male	Test Group	50 Mg/Kg
	As-Iii	Aw Rat	Male	Test Group	300 Mg/Kg
	As-Iv	Aw Rat	Male	Test Group	2000 Mg/Kg
Balanitesa Egyptiaca	Be-I	Aw Rat	Male	Test Group	5 Mg/Kg
	Be-Ii	Aw Rat	Male	Test Group	50 Mg/Kg
	Be-Iii	Aw Rat	Male	Test Group	300 Mg/Kg
	Be-Iv	Aw Rat	Male	Test Group	2000 Mg/Kg
Gloriosa Superb	Gs-I	Aw Rat	Male	Test Group	5 Mg/Kg
	Gs-Ii	Aw Rat	Male	Test Group	50 Mg/Kg
	Gs-Iii	Aw Rat	Male	Test Group	300 Mg/Kg
	Gs-Iv	Aw Rat	Male	Test Group	2000 Mg/Kg
Tagetes Erecta	Te-I	Aw Rat	Male	Test Group	5 Mg/Kg
	Te-Ii	Aw Rat	Male	Test Group	50 Mg/Kg
	Te-Iii	Aw Rat	Male	Test Group	300 Mg/Kg
	Te-Iv	Aw Rat	Male	Test Group	2000 Mg/Kg
Cyathocline Purpurea	Cp-I	Aw Rat	Male	Test Group	5 Mg/Kg
	Cp-Ii	Aw Rat	Male	Test Group	50 Mg/Kg
	Cp-Iii	Aw Rat	Male	Test Group	300 Mg/Kg
	Cp-Iv	Aw Rat	Male	Test Group	2000 Mg/Kg

4.5.1 Acute Oral Toxicity (Oecd 423)

The Acute Toxic Class Method Set Out In This Guideline Is A Stepwise Procedure With The Use Of 3 Animals Of A Single Sex Per Step. Depending On The Mortality And/Or The Moribund Status Of The Animals, On Average 2-4 Steps May Be Necessary To Allow Judgment

On The Acute Toxicity Of The Test Substance. The Substance Is Administered Orally To A Group Of Experimental Animals At One Of The Defined Doses. The Substance Is Tested Using A Stepwise Procedure, Each Step Using Three Animals Of A Single Sex. Absence Or Presence Of Compound-Related Mortality Of The Animals Dosed At One Step Will Determine The Next Step, I.E., No Further Testing Is Needed, Dosing Of Three Additional Animals, With The Same Dose And, Dosing Of Three Additional Animals At The Next Higher Or The Next Lower Dose Level. Three Animals Are Used For Each Step. The Dose Level To Be Used As The Starting Dose Is Selected From One Of Four Fixed Levels, 5, 50, 300 And 2000 Mg/Kg Body Weight [16].

4.7 *In Vivo* Carrageenan-Induced Paw Edema

This Anti-Inflammatory Test Was Performed According To The Method Of Seewaboon Et Al., 2010 With Slight Modification. Edema In The Left Hind Paw Of Rat Was Induced By Injection 0.05 Ml Of 1% (W:V) Carrageenan (Sigma, St Louis, Mo) In Saline Into The Footpad, Subscutaneously The Paw Diameter Were Determined Using A Digital Vernier Caliper Prior To And 1, 3 And 5 H After Carrageenan Injection. The Drug Test Groups Were Treated With Extract (200 And 400 Mg/Kg Body Weight, P.O.) 1 H Before Carrageenan Injection. The Animals In The Control Group Received Saline Only. Another Group Of Rats Was Administered With Indomethacin (10 Mg/Kg, I.P.) In Distilled Water As A Standard Reference. The Anti-Inflammatory Activity Was Calculated As Percentage Inhibition Of Carrageenan Induced Paw Edema Using The Following Formula.

Percent Inhibition= [1- Paw Diameter In Treated (Dt)/Paw Diameter In Control (Dc)] X 100.

Table: 3 Treatment Group And Doses For Carrageenan-Induced Paw Edema

S. No.	Groups	Treatment
1	Control Group	1% Carrageenan Solution (5 Ml /Kg B.W)
2	Standard Group	Carrageenan + Indomethacin (10 Mg/Kg B.W)
3	Treatment Group-I	Carrageenan + As Extract (200 Mg/Kg), Orally
4	Treatment Group-Ii	Carrageenan + As Extract (400 Mg/Kg), Orally
5	Treatment Group-Iii	Carrageenan + Be Extract (200 Mg/Kg), Orally
6	Treatment Group-Iv	Carrageenan + Be Extract (400 Mg/Kg), Orally
7	Treatment Group-V	Carrageenan + Gs Extract (200 Mg/Kg), Orally
8	Treatment Group-Vi	Carrageenan + Gs Extract (400 Mg/Kg), Orally
9	Treatment Group-Vi	Carrageenan + Te Extract (200 Mg/Kg), Orally
10	Treatment Group-Viii	Carrageenan + Te Extract (400 Mg/Kg), Orally
11	Treatment Group-Ix	Carrageenan + Cp Extract (200 Mg/Kg), Orally
12	Treatment Group-X	Carrageenan + Cp Extract (400 Mg/Kg), Orally

Screening Method For Analgesic Activity

Tail Flick Method

Weigh And Divide The Mice In Five Groups. Group I Will Work As Vehicle Treated, Group Ii Will Work As Standard Drug Treated, Group Iii, Iv & V Will Receive Extracts Of Selected Plants. The Reaction Time Will Get Record By Using Tail Flick Analgesiometer At Different Time Interval After The Drug Administration.

Eddy's Hot Plate Method

Weigh And Divide The Mice In Five Groups. Group I Will Work As Vehicle Treated, Group Ii Will Work As Standard Drug Treated, Group Iii, Iv & V Will Receive Extracts Of Selected Plants. The Latency To Flick The Hind Paw Or Lick Or Jump From The Hot Plate Is The Reaction Time Here. The Reaction Time Will Get Record By Using Eddy's Hot Plate Instrument At Different Time Interval After The Drug Administration.

Table 4: Treatment Group And Doses For Tail Flick & Eddy's Hot Plate Method

S. No.	Groups	Treatment
1	Control	10 Ml/Kg B.W
2	Standard	Diclofenac Sodium (10 Mg/Kg B.W)
3	Group-I	As Extract (200 Mg/Kg), Orally
4	Group-Ii	As Extract (400 Mg/Kg), Orally
5	Group-Iii	Be Extract (200 Mg/Kg), Orally
6	Group-Iv	Be Extract (400 Mg/Kg), Orally
7	Group-V	Gs Extract (200 Mg/Kg), Orally
8	Group-Vi	Gs Extract (400 Mg/Kg), Orally
9	Group-Vii	Te Extract (200 Mg/Kg), Orally
10	Group-Viii	Te Extract (400 Mg/Kg), Orally
11	Group-Ix	Cp Extract (200 Mg/Kg), Orally
12	Group-X	Cp Extract (400 Mg/Kg), Orally

5.7.9 Statistical Analysis

Results Were Expressed As Mean ± Sem. Statistical Analysis Was Performed Using One-Way Analysis Of Variance (Anova) Followed By Dunnett's Test. $P < 0.05$ Was Considered Statistically Significant.

Result & Discussion

***In-Vivo* Experiment**

Table 5: Showing Results Of Acute Oral Toxicity (Oecd)

Plant Used	Group No.	Dose (Mg/Kg Body Weight)	Observations/ Mortality
Argyreia Speciosa	As-I	5 Mg/Kg	0/3
	As-Ii	50 Mg/Kg	0/3

	As-Iii	300 Mg/Kg	0/3
	As-Iv	2000 Mg/Kg	0/3
Balanitesa Egyptiaca	Be-I	5 Mg/Kg	1/3
	Be-Ii	50 Mg/Kg	0/3
	Be-Iii	300 Mg/Kg	0/3
	Be-Iv	2000 Mg/Kg	0/3
Gloriosa Superb	Gs-I	5 Mg/Kg	1/3
	Gs-Ii	50 Mg/Kg	0/3
	Gs-Iii	300 Mg/Kg	0/3
	Gs-Iv	2000 Mg/Kg	0/3
Tagetes Erecta	Te-I	5 Mg/Kg	0/3
	Te-Ii	50 Mg/Kg	1/3
	Te-Iii	300 Mg/Kg	0/3
	Te-Iv	2000 Mg/Kg	0/3
Cyathocline Purpurea	Cp-I	5 Mg/Kg	0/3
	Cp-Ii	50 Mg/Kg	0/3
	Cp-Iii	300 Mg/Kg	0/3
	Cp-Iv	2000 Mg/Kg	0/3

In Case Of Acute Oral Toxicity Study When Animals Were Treated With 5, 50, 300, And 2000 Mg/Kg B.W. Of Dose. There Was No Mortality And Any Behavioural Changes Thus Selected Dose Will Be On The Basis Of Ld_{50}, 200 And 400 Mg/Kgb.W.

Carrageenan-Induced Paw Edema

The Anti-Inflammatory Activity Of *Argyreia Speciosa, Balanitesa Egyptiaca, Gloriosa Superb, Tagetes Erecta & Cyathocline Purpurea* Against Carrageenan Induced Paw Edema Has Been Shown In And The Results Were Comparable To That Of Standard Drug Indomethacine, A Pro-Type Of Non-Steroidal Anti-Inflammatory Agent. The *Balanitesa Egyptiaca* Extract Showed Maximum Paw Volume Of 2,395 At The Dose 200 Mg/Kg Body Wt. After Extract Treatment In Carrageenan Induced Paw Edema Whereas The Reference Drug (Indomethacine) Produced.

Table 6: Showing Results Of Carrageenan-Induced Paw Edema

Treatment Groups	**Paw Volume**		
	1 Hr	**3 Hr**	**5 Hr**
Control	1.567±0.304	1.780±0.278	2.395± 0.199
Standard (Indomethacine)	0.770±0.111	0.667±0.104	0.427± 0.073
Treatment Group-I	1.497±0.144	1.285±0.025	1.232±0.419
Treatment Group-Ii	1.135±0.040	1.037±0.040	0.867±0.086
Treatment Group-Iii	1.457±0.304	1.940±0.278	2.395± 0.199
Treatment Group-Iv	0.830±0.111	0.567±0.104	0.427± 0.073
Treatment Group-V	1.597±0.144	1.223±0.025	1.232±0.419

Treatment Group-Vi	1.145±0.040	1.027±0.040	0.967±0.086
Treatment Group-Vi	1.367±0.304	1.850±0.278	2.105± 0.199
Treatment Group-Viii	0.890±0.111	0.757±0.104	0.537± 0.073
Treatment Group-Ix	1.447±0.144	1.325±0.025	1.232±0.419
Treatment Group-X	1.193±0.040	1.077±0.040	0.887±0.086

Table 7: Showing Results Of Tail Flic Method

		Reaction Time In Sec					
Groups	**Dose**	**0 Min**	**30 Min**	**60 Min**	**90 Min**	**120 Min**	**180 Min**
Control	10 Ml/Kg	2.00±0.258	3.00±0.258	3.60±0.211	4.50±0.341	5.50±0.341	6.30±0.333
Standard Diclofenac Sod.	10 Mg/Kg	3.16±0.166	4.16±0.307	4.50±0.342	5.16±0.401	6.33±0.557	7.00±0.258
Group-I	As 200 Mg/Kg	2.36±0.336	3.19±0.310	4.69±0.342	4.71±0.342	4.85±0.307	5.89±0.307
Group-Ii	As 400 Mg/Kg	2.83±0.172	3.38±0.218	3.87±0.324	4.84±0.341	5.20±0.141	6.04±0.167
Group-Iii	Be 200 Mg/Kg	2.51±0.154	3.67±0.445	3.96±0.251	4.14±0.484	4.24±0.238	4.87±0.643
Group-Iv	Be 400 Mg/Kg	2.67±0.174	3.85±0.228	4.36±0.217	4.76±0.324	5.09±0.168	5.42±0.188
Group-V	Gs 200 Mg/Kg	1.44±0.132	1.88±0.214	2.24±0.252	2.87±0.411	3.27±0.634	4.23±0.141
Group-Vi	Gs 400 Mg/Kg	2.81±0.156	3.23±0.115	3.45±0.311	4.25±0.245	4.86±0.167	5.40±0.241
Group-Vii	Te 200 Mg/Kg	2.85±0.152	3.24±0.441	3.76±0.222	4.56±0.855	4.85±0.527	5.21±0.153
Group-Viii	Te 400 Mg/Kg	3.21±0.241	3.84±0.248	4.21±0.425	4.45±0.417	4.89±0.124	5.45±0.195
Group-Ix	Cp 200 Mg/Kg	1.45±0.154	1.89±0.146	2.24±0.244	3.33±0.251	3.80±0.214	4.43±0.221
Group-X	Cp 400 Mg/Kg	3.26±0.141	3.74±0.254	3.93±0.247	4.16±0.411	4.54±0.254	5.16±0.527

Table 8: Showing The Results Of Eddy's Hot Plate Method

		Reaction Time In Sec					
Groups	**Dose**	**0 Min**	**30 Min**	**60 Min**	**90 Min**	**120 Min**	**180 Min**
Control	10	4.00±0.	4.83±0.1	5.33±0.2	6.33±0.2	6.50±0.2	7.33±0.2

	Ml/Kg	258	66	11	11	24	11
Standard Diclofenac Sodium	10 Mg/Kg	5.16±0.166	5.50±0.224	6.33±0.211	7.16±0.211	7.50±0.224	8.16±0.307
Group-I	As 200 Mg/Kg	4.33±0.333	5.16±0.307	5.66±0.333	6.66±0.333	6.83±0.307	7.83±0.307
Group-Ii As 400	As 400 Mg/Kg	4.80±0.167	5.33±0.210	5.83±0.307	6.83±0.307	7.16±0.166	8.00±0.166
Group-Iii	Be 200 Mg/Kg	4.52±0.152	5.61±0.425	5.94±0.231	6.04±0.485	6.23±0.237	6.97±0.653
Group-Iv	Be 400 Mg/Kg	4.73±0.182	5.88±0.218	6.30±0.215	6.75±0.327	7.04±0.167	7.40±0.187
Group-V	Gs 200 Mg/Kg	3.48±0.133	3.89±0.217	4.26±0.254	4.89±0.412	5.28±0.632	6.23±0.149
Group-Vi	Gs 400 Mg/Kg	4.81±0.156	5.23±0.115	5.45±0.311	6.25±0.245	6.86±0.167	7.40±0.241
Group-Vii	Te 200 Mg/Kg	4.85±0.152	5.24±0.441	5.76±0.222	6.56±0.855	6.85±0.527	7.21±0.153
Group-Viii	Te 400 Mg/Kg	5.21±0.241	5.84±0.248	6.21±0.425	6.45±0.417	6.89±0.124	7.45±0.195
Group-Ix	Cp 200 Mg/Kg	3.45±0.154	3.89±0.146	4.24±0.244	5.33±0.251	5.80±0.214	6.43±0.221
Group-X	Cp 400 Mg/Kg	5.26±0.141	5.74±0.254	5.93±0.247	6.16±0.411	6.54±0.254	7.16±0.527

Discussion And Conclusion

In Order To Provide A Scientific Explanation For The Folk Use Of *Argyreia Speciosa, Balanitesa Egyptiaca, Gloriosa Superb, Tagetes Erecta & Cyathocline Purpurea*, We Have Investigated The Biological Effects Of Its Extracts, Mainly The Ones Related To The Inflammatory Process.

Medicinal Plants Play A Crucial Role In World Health. Even Though There Is An Immense Growth In Modern Medicine; Plants Still Make An Important Contribution To Health Care. Phytochemical Screening Is Planned To Separate Specific Plant Constituents To Evaluate Their Biological Activity Or Medicinal Uses. Plant's Medicinal Value Is Because Of The Presence Of Particular Chemical Substances That Have A Definite Physiological Action On The Living System [18]**.**

Qualitative Phytochemical Screening Showed The Presence Of Active Metabolites Such Assaponins, Alkaloids, Glycosides And Phenols.

In Acute Toxicity Study, Oral Administration Of The Crude Extracts Of *Argyreia Speciosa, Balanitesa Egyptiaca, Gloriosa Superb, Tagetes Erecta & Cyathocline Purpurea* (Up To 2000 Mg/Kg) And The Revealed Its Non-Toxic Nature.

The Present Data Clearly Showed That Extract Of *Balanitesa Egyptiaca* (200 Mg/Kg Bw) Have Anti-Inflammatory Activity By The Highly Significant Responses Of Some Extracts On Inhibiting The Edema Formation After Carrageenan Sub Plantar Injection. The Extracts Which Showed The Highest Anti-Inflammatory Activity, Presented Also Highly Significant Statistic Values For Carrageenan Induced Edema Inhibition After The Treatment With The Phlogistic Agent. It Is Evident That Carrageenan Is A Sulphated Polysaccharide Obtained From Sea Weed (Rhodophyceae) And Is Commonly Used To Induce Acute Inflammation. The First Phase Is Due To Release Of Histamine And Serotonin. Carrageenan-Induced Rat Paw Edema Model Is A Suitable Test For Evaluating Anti-Inflammatory Drugs, Which Has Frequently Been Used To Assess The Anti Edematous Effect Of The Drug. Carrageenan Is A Strong Chemical Use For The Release Of Inflammatory And Pro Inflammatory Mediators (Prostaglandins, Leukotrienes, Histamine, Bradykinin, Tnf-A, Etc.) The Course Of Acute Inflammation Is Biphasic. First Phase Starts With The Release Of Histamine, Serotonin, And Kinins After The Injection Of Phlogistic Agent In The First Few Hours. While The Second Phase Is Related To The Release Of Prostaglandins Like Substances In 2-3 Hours. Second Phase Is Sensitive To Both The Clinically Useful Steroidal And Non Steroidal Anti-Inflammatory Agent. Prostaglandins Are The Main Culprit Responsible For Acute Inflammation. Lactobacillus Sp Might Be Containing Some Anti-Inflammatory Agent Which Is Responsible For The Blockage Of Prostaglandins And Inflammatory Pathway [19].

These Mediators Take Part In Inflammatory Response And Are Able To Stimulate Nociceptive And Thus Reduce Pain. It Has Been Reported That Second Phase Of Oedema Is Sensitive To Most Clinically Effective Anti Inflammatory Drugs, Which Has Been Frequently Used To Access The Anti-Oedematous Effect Of Natural Products. Based On These Reports, It Can Be Inferred That The Inhibition Effect Of The Extract Of *Balanitesa Egyptiaca* On Carrageenan Induced Inflammation In Mice May Be Due To Inhibition Of The Mediators Responsible For Inflammation [20].

Knowledge On The Immune-Mediated Mechanisms In Metabolic Scenario Has Markedly Increased In The Recent Past, Evidencing The Role That Dietary Components May Have To Modulate Immunity By Enhancing Or Suppressing The Immune Response. For Instance, Certain Strains Of Probiotics Have Been Demonstrated To Be Able To Modulate The Immune System By Stimulating Release Of Different Patterns Of Cytokines By Different Cells. It Could Be Able To Modify The Number Of Cd_4 T Cells And Actively Interfere With Anti-Inflammatory And Pro Inflammatory Signaling Pathways By Inducing Production Of Il-10 And Reducing Inf-Γ And Tnf-A Release. Herbal Drugs Modulate Both Innate And Acquired Immunity By Interacting With Host Mucosal Cells To Induce Or Modulate The Immune Response. This Can Be Another Possible Reason Behind Its Anti-Inflammatory Property In This Study [21].

The Hot-Plate And Tail Flick Tests Are Useful In Elucidating Centrally Mediated Antinociceptive Responses, Which Focuses Mainly On Changes Above The Spinal Cord Level. The Significant Increase In Pain Threshold Produced By In These Models Suggests Involvement Of Central Pain Pathways. Pain Is Centrally Modulated Via A Number Of Complex Processes Including Opiate, Dopaminergic, Descending Noradrenergic And Serotonergic Systems. The Analgesic Effect Produced By The Extract May Be Via Central Mechanisms Involving These Receptor Systems Or Via Peripheral Mechanisms Involved In The Inhibition Of Prostaglandins, Leucotrienes, And Other Endogenous Substances That Are Key Players In Inflammation And Pain. The Extract Gave A Similar Effect On The Formalin Test Inhibiting Both The First And The Second Phase. Formalin Test Is Biphasic, And Measures Pain Of Both Neurogenic (First Phase) And Of Inflammatory Origin (Second Phase). The First Phase (0 – 5min) Being A Result Of Direct Stimulation Of Nociceptors Measures Centrally Mediated Effects And Is Insensitive To Anti-Inflammatory Agents While The Second Phase (15-30 Min) Which Is Qualitatively Different From The First Phase Is Dependent On Peripheral Inflammation And Changes In Central Procession Due To Chemical Mediators Release From Damaged Cells That Stimulate Nociception And Thus Induced Pain.

The As 400 Mg/Kg Show Significant Increase In Latency To Flick Tail Compared To Control Group ($P > 0.05$). The Highest Nociception Inhibition Of Stimulus By As 400 Mg/Kg (400 Mg/Kg) Was Observed Up To 180 Minutes. In Case Of Ethanolic Extract Of *Argyreia Speciosa*, The Analgesic Activity Profile Of All The Extracts Of 200 & 400 Mg/Kg Showed Significant When Compared To All Other Plant Extracts With Different Doses.

Eddy's Hot Plate Method For Analgesic Activity

The As 400 Mg/Kg Show Significant ($P> 0.05$) Increase In The Mean Basal Reaction Time In Hot Plate Method Compared To Control And Other Treatment Groups. The As 200 Mg/Kg Of *Argyreia Speciosa* At Dose (200 Mg/Kg, P.O.) Also Showed Significant ($P < 0.05$) Increase In The Mean Basal Reaction Time. The Highest Nociception Inhibition Of Stimulus Exhibited By As 400 Mg/Kg *A. Speciosa* (400 Mg/Kg) Was Observed Up To 180 Minutes.

Conclusion

The Result Of The Present Investigation Revealed That The Parts Of Plants Used Possess A Moderate Anti-Inflammatory Effect That Was Evidenced By The Significant Reduction In Paw Edema And Hot Plate, Tail Flick Methods. Carrageenan Is A Sulphated Polysaccharide Obtained From Seaweed (Rhodophyceae) Which Is Commonly Used To Induce Acute Inflammation And Is Believed To Be Biphasic. The First Phase Is Due To Release Of Histamine And Serotonin. The Second Phase Is Caused By The Release Of Bradykinin, Protease, Prostaglandin And Lysosome. It Has Been Reported That The Second Phase Of The Edema Is Sensitive To Most Clinically Effective Anti-Inflammatory Drugs, Which Has Frequently To Access The Anti-Edematous Effect Of Natural Products. Prostaglandins Play A Major Role In The Development Of The Second Phase Of The Reaction, Which Is Measured At Around 3 Hours Time. The Carrageenan-Induced Paw Edema Model In Rats Is Known To Be Sensitive To Cyclo-Oxygenase (Cox) Inhibitors And Has Been Used To Evaluate The Effects Of Non-Steroidal

Anti-Inflammatory Agents Against Which Primarily Inhibits The Enzyme Cox Involved In Prostaglandin Synthesis. Based On The Results, It Can Be Inferred That The Inhibitory Effect Of Extracts On Carrageenan-Induced Inflammation In Rats May Be Due To The Inhibition Of Enzyme Cyclo-Oxygenase. The Present Results Suggest That Ethanolic Extract Of *Balanitesa Egyptiaca* Suppresses The First Phase Of Carrageenan-Induced Paw Edema, Thus, Confirming An Nsaid-Like Property.

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