International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1351-1359 www.ijprajournal.com ISSN: 2249-7781

"Evaluation Of Antiulceractivity Of Methanol Aqueous Flow Extract Of Canthium Dicoccum Line In Male Wistar Albino Rats"

Yousif Alballa *Ms. Sarita Sharma. * Dr. Gaurav Kumar Sharma. * Dr. Kaushal K Chandrul.
Student of b. Pharmacy 4th year, Assistant Professor, H.O.D., Principle
Department of pharmacy
Mewar university, chittorgarh india

Date of Submission: 01-08-2021 Date of Acceptance: 18-08-2021

ABSTRACT
Investigationofthe Nephroprotectiveactivity ofethanol extractof FicusdalhousiaeonGentamicininduced nephrotoxicityinmaleWistarrats.Inthismodelofnephrotoxicity,30adultmalewistarrats(150-200gms)wereevenlydividedinto5groups.Group-1and Group-2served asuntreatedand model controls respectively,whileGroup3,4and5werethetreatmentsgroupswhichweresimultaneouslytreatedwithstandard,200and400mg/kgextract respectively,after each dose gentamicin (80mg/kg,i.p.)for 10day on11th day,blood samples for biochemical parameters,while the rats kidneys forhistology were obtained under inhaled diether anaesthesia. Gentamicin treatment caused nephrotoxicityasevidenced bymarked elevation inblood urea,uricacidand creatinine.Co-administrationofextract withParacetanmoldecreasedriseinbloodurea, uricacidand creatinine.Apartfromthese,histopathologicalchanges alsoshowed the protectivenature of extract against Gentamicin induced necrotic damage of renal tissues.Itwasobservedthat theethanol extract ofconferrednephroprotectiveactivity byhistopathologicalandbiochemicalobservation againstGentamicininduced nephrotoxicityinrats.Inthenearfuture couldconstitutealeadtodiscovery ofanovel drugfortreatmentofdruginducednephrotoxicity.

I. INTRODUCTION

Apeptic ulcerisanopen craterorsore that develop in the inner lining (mucosa)of the stomach or the duodenum. A coating of mucus and otherchemicals normallyshieldsthe stomach and duodenumfrom digesting themselves. Whenthese protective mechanismsaredisrupted, powerful digestive acidscanerode intothelining ofthese organs and cause peptic ulcer. Peptic ulcer isamajor gastro-intestinal disordercaused by an imbalance between offensive(gastric acid, pepsinogen secretion)anddefensive (mucussecretion, gastricmucosal integrity)factors.Itisaround or oval sore where theliningofthestomach or duodenum hasbeeneaten awayby stomachacidanddigestivejuices.

PATHOPHYSIOLOGY OF PEPTIC ULCER

Theterm peptic ulcer refers tochronic ulcerativedisorderofthe upper gastro intestinaltract,which have acommon participationof acidandpepsin intheir pathogenesis.Itincludes duodenalulcer andgastriculcer,aswellas, ulcer associated withZollinger-Ellison syndrome.Itisaphysiologicmarvelthat gastricjuice caneasilydigestthe swallowed pieces ofmeat but normally has no corrosiveaction on the gastric mucosaitself.Several factors seen tobe involved intheprotectionofthegastric mucosa fromauto digestion.These factors,collectivelytermed gastric mucosalbarrierinclude

(a) Mucussecretedbythesurface epithelial cellsandmucous neck cells which forms a water insolate visco-elastic gell with poordiffusionco-efficientforH^+

(b)Bicarbonatesecretedbysurface epithelial cellsintotheboundary zonebetweenepithelial cellsand themucuslayer. Thesecretionof mucusandbicarbonateseems to bemedicated through prostaglandins.

(c) Tight junctions between the adjacent cellsofepithelium

(d)Rapid turnover of the surface epithelial cellsand richmucosal bloodsupply

(e) Prostaglandins

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1351-1359 www.ijprajournal.com ISSN: 2249-7781

Endogenous prostaglandins stimulate secretionof gastricmucusaswellas gastric and duodenal mucosal bicarbonate.Theyalsoparticipateinthe maintenanceof gastricmucosalblood flow and integrity of mucosal barrier and promoteepithelial cellsrenewalin response to mucosal injury. A breakdownofthe balance betweenthe corrosiveaction ofacid-pepsinand the mucosalresistance resultsinpeptic ulcers.Induodenalulcer or ulcers due toZollinger-Ellison syndrome,evidence ofanabsoluteoratleast relative gastric hypersecretioncanbedemonstrated. In contrast, defectivemucosalresistance seemstobemajorcontributory factorin gastriculcers.Itislesscommonthanthe DU.A directgastricmucosalinjuryisthe most importantfactor in the pathogenesisofGU. Manycases ofGU havehyposecretionofgastric acidwith secondaryslightlyincreased gastrin secretion (feedback effect).Gastric emptying term isoften delayed.GU always occurs inthe nonacidsecreting portion of the stomach, often at the lesser curvature.InfectionbyH.pyloriis also implicated in the pathogenesisof GU. History of chronic ingestion of aspirin orother non-steroidal anti- inflammatorydrug(NSAIDS)aspresent in15-25% casesofGU.Thesedrugs are believedtoactbydepletion of prostaglandinsmedicated protective mechanismsingastricmucosa.

SCREENING METHODOLOGIESFOR ANTIULCERACTIVITY

INVIVOMETHODS

Pylorusligation inrats(SHAY)

Male orFemaleWistarstrain albinorats weighing 150-170g are starvedfor 48 hrs, havingaccesstodrinking water and libitum. During this time they are housed single in cages with raised bottomsofwide wire mesh inorder to avoid cannibalismand coprophagy.Six animals are used per dose and as controls.Under ether anesthesiaa midlineabdominal incisionismade.The pylorus isligated,care being exercised thatneitherdamage tothebloodsupply nortraction onthepylorusoccurs. Graspingthestomach withinstruments istobemeticulously avoided;else ulceration will invariably develop at such points. The abdominal wall is closed bysutures.Thetest compounds are given either orally by gavage or injectedsubcutaneously.

The animals are placed for 19hrs in plasticcylinders withaninner diameter of45mmbeingclosedonbothends by wire mesh.Afterwards,the animals are sacrificed in CO_2 anesthesia. The abdomen is opened and a ligature is placed aroundthe esophagusclose to thediaphragm. Thestomach isremoved andthecontentsaredrained ina centrifuge tube.Along thegreater curvature thestomach isopened and pinned onacork plate.Themucosa is examined with a stereomicroscope. In the rat, the upper two fifths of the stomach form the Lumen with squamousepitheliumand posses little protectivemechanisms against the corrosiveactionof gastricjuice.Belowa limiting ridge,inthe glandularportion ofthe stomach,the protective mechanismsare betterinthemucosaof the medium two fifths ofthe stomach than in the lower part, forming the antrum. Therefore,lesions occurmainly in the lumen and in the antrum. The number of ulcers is noted and the severity recorded withthefollowing scores: O= no ulcers 1 = superficial ulcers2 =deep ulcers 3 =perforation. Thevolumeofthegastriccontent is measured. After centrifugation, acidity is determined by titrationwith 0.1 N NaOH.

INVITROMETHOD

Theeffectsofcertain antiulceragentson the antimicrobialactivity ofantibiotics effective against H.Pylori were determinedIn-vitro. Helicobacter.Pylori werecultured onSkirrow'sagar. Amoxycillin Clarithromycin, Erythromycin&Tetracycline were used. The Antiulcer agents studied by measuringthe ureaseactivity. Urease activitywasmeasured bytheurease- indophenol method. Theminimum inhibitory concentration was determinedby a plating method,with H.pylori streakedon plates containing
various concentrationsof theantibiotics plussublethaldosesof theantiulcer agents,which maybeevaluatedforthe Antiulceractivity.

PlantprofileofCanthiumdicoccum Botanical Name: Canthiumdicoccum (Gaertn.)Merr.**Family:**Rubiaceae; **CommonName:** Bogas (P.Bis.),Luing- luing (P.Bis.), Malakafe (P.Bis.), Tandan(Mag.), Ceylonboxwood (Engl.); **Vernacular Name:**TAMIL: Nallamandharam; **Habit and Habitant:**Malakafe is anunarmed, smooth shrub 3 to 4 metersor more inheight.**Leaves**are extremelyvariable,

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1351-1359 www.ijprajournal.com ISSN: 2249-7781

ovate,elliptic, ovate or somewhat rounded,5to15centimeterslong,1.5to 10 centimeterswide,leathery,shining above,andusuallypointedatboth ends. **Flowers** are white, withvery slender stalks, 5 to 10 millimeters long and borne incompressed, short-stalked cymes.Calyxis cutoffattheendor obscurelytoothed.Corollaisbell-shaped, witha 4-to 6-millimetertube,and five somewhatpointedlobes.

II. MATERIALS AND METHODS

Diclofenacsodium- 400mg/kg(Asha analytical Pvt. Ltd ,Uppal,Hyd), Ranitidine- 13.5 mg/kg (Vinallabs,Yadgirigutta),NaOH (Asha analytical Ltd,Uppal,Hyd), Topfers reagent(Nice, chemicalsPvtLtd,Cochin), Formalin10%(Asha analytical PvtLtd,Uppal,Hyd),Tween 80 2%(Asha analyticalPvtLtd,Uppal,Hyd), Distilled water

Collectionofplantmaterial

TheFlowers ofCanthiumdicoccumused for the present studies was collected from Chitoor district of Andhra pradesh. Theplantwasidentified, confirmed andauthenticated by comparing withvoucher specimen availableatSurveyofmedicinalplants&collection unit,Department of Botany, Sri Venkateswara University,Tirupathi byFieldBotanist Dr.Madhavshetty.The barkwascut intosmallpiecesandshade dried. Thedriedmaterial wasthen pulverized separately into coarse powder byamechanichalgrinder.The resulting powderwasthenusedfor extraction.

PreparationofMethanolicExtract

Thepowdered drug was dried and packed well in Soxhlet apparatusand extractedwith1500 mlofmethanolfor seven days. The extract was concentrated and dried using Rotary flash evaporator. It was kept in desiccatorsuntilused.

III. EXPERIMENTAL ANIMALS

Swiss Albino rats adult of either sex were obtained from Mahaveer enterprises, Hyd(169/CPCSEA/1999). Therats were divided randomlyinto 4 groups of5 rats each for each model. Eachratthatweighed between180-200 gm was housed separately (Four rats per cage).Theanimals were leftfor48 hrsto acclimatizeto theanimalroom conditions.Theyweremaintained in standardlaboratoryconditions of temperature22±2^{o}c,humidity, 12hours lightand dark cyclesfedwith standard pellet diet (Hindustanlever,Bangalore) andadequatetapwater.

METHODS

The rats are divided into different groups eachcomprising of minimum of fiveratsasdetailed below

GroupI – Control rats (Diclofenac +tween80)

GroupII–Diclofenacinduced ulcerrats orally treated with Ranitidine (13.5 mg/kgb.w)

Group III– Diclofenac induced ulcer ratsorallytreated with formulation(Canthiumdic occum) at the dose of 200 mg/kgb.w(SINGLE DOSE)

Group IV– Diclofenac induced ulcer ratsorallytreated with formulation (DOUBLE DOSE)

Theanimal inallthe groups were kept for24 h.fastingafter that animal ofall groups'receiveddiclofenac sodium (NSAIDs, 20mg/kg).

Theoralfeedingof water anddiclofenac sodiumwas continuedfor3days, theanimalof II,III and IVwere administered with ranitidine(13.5mg/kg),flower extract (200mg/kg), flower extract (400mg/kg)respectivelyafter 3 h.ofdiclofenac sodiumadministration.On 4thday the animalsweresacrificed, stomach were removed andcutalongthe greatercurvatureto measure theulcerindex.

EVALUATIONPARAMETERS

CollectionofGastricJuice

The stomach was excised carefully keeping the esophagusclosed,opened along the greater curvature and the gastriccontents wereremoved. The gastric contentswere collected inplain tubesandcentrifuged at3000rpmfor5 min;thevolumeof thesupernatantwas expressedas ml/100gmbody weight. The mucosawasflushedwithsalineand observed forgastriclesionsusinga dissecting microscope,ulcer score was determined.

UlcerScoring

Aftersacrificingtherat, stomach was removed and opened alongthe greater curvature,and washed itslowly under running tap water. Put itonthe glass slide and observe under 10X magnification forulcer. Scoretheulcers asbelow.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1351-1359 www.ijprajournal.com ISSN: 2249-7781

0=normalcoloured stomach
0.5=redcolouration
1=spotulcers
1.5=haemorrhagicstreaks
2=Ulcers≥3but≤5
3=Ulcers>5
Mean ulcer score for each animal is expressedasUlcerIndex.

FreeacidityandTotalacidity Centrifugethe gastric contentsat1000 rpm for 10 min, note the volume. Pippete out 1mlofsupernatantliquid and dilute it to 10 ml with distilled water.Notethe P^Hofthe solution with thehelpofP^Hmeter.Titrate thesolution against 0.01NNaOH using topfers reagentas an indicator.(ItisDimethyl- amino-azo-benzene with phenolphthaleinand used fordetection andestimationofhydrochloricacidand total acidity ingastric fluids) Titrate to end point when the solution turns to orangecolour.NotethevolumeofNaOH which corresponds to free acidity. Titrate furthertillthe solution regains itspinkcolour.Notethetotalvolumeof NaOHwhich corresponds to the total acidity.Acidity(mEq/1/100g)canbe expressedas:

Acidity =

$$\frac{Vol.of\ NaOH \times Normality \times 100}{0.1}$$

mEq/l/100g

Statisticalanalysisofdata
Resultswereexpressedasmean±S.E.M.
Thestatisticaldifference between the groups inthe term ofthe mean rate of wound healing was calculated interms ofANOVAmean ±S.E.M.Thedifference wasconsideredsignificantifP<0.05.

PHARMACOLOGICALSTUDIES DICLOFENAC SODIUM INDUCED ULCERS
Effect ofGastricVolume
Administration of the extract significantly decreased the gastric volumeincomparisonwithrats treated with Ranitidine.Comparingthe gastric volume and gastric acidity,the gastric volume gets decreased,simultaneously thegastricacidityalso decreased significantly.

Effect of Free Acidity and Total Acidity
The free acidity and total acidity was determined based on the titre values. The free acidity and total acidity of extract on albino rats decreased significantly in comparison with the standardgrouptreatedwithRanitidine. **Ulcerindex**
Theulcerindexwascalculated bytaking the mean ulcer score of each groups.Thenthemeanulcerscoregraph was plotted with groups onx-axisand ulcer indexony-axis.Thehistogramsof different groups were then interpolated bycomparingtheulcerindexofgroup I with group II,IIIand IV.Itwasnoticed that the ulcer index of Dose group (Dose-III&IV) was significantly less when comparedto the standardgroup (Group-II)treatedwithRanitidine.

DISCUSSION
Before screening the test extract for antiulcerprotectiveactivity,the extract was subjected to the acute toxicity studies as per OECD guidelines no.420(fixeddose method). Theextract wasfoundtobenon-toxicat2000mg/kg as indicated by the mortality in the treatedgroup. Hence, the 2000mg/kg was treatedas cut offtolerable dose, $1/10^{th}$ (200mg/kg), and $1/5^{th}$ (400mg/kg)ofthis dose were selected forthefurtherstudy.
It is evident from the result of the present investigation that the formulationof Canthiumdicoccum possessesantiulceractivityindiclofenac inducedacuteulcermodel.Ithasshown asignificantreduction inthegastric lesions in both the models. Although the etiology of gastric ulcer is not knowninmostcases, itisgenerally accepted that it resultsfrom an imbalance between aggressive factors and the maintenance of mucosal integrity through the endogenous defencemechanisms. To regainthe balance, different therapeuticagents includingplantextracts areused(in experimental animals) to inhibit the gastricacidsecretion ortoboostthe mucosaldefencemechanisms by increasingmucusproduction,stabilizing thesurfaceepithelial cells/or enhancing prostaglandin synthesis. Ranitidine the proton pump inhibitor play an important role in the reduction of gastricvolumeand totalacidity and thus perform acytoproectiveeffect. The presentresults demonstratethatthe formulation of Canthiumdicoccum protectthe rat gastric mucosa against hemorrhagic

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1351-1359 www.ijprajournal.com ISSN: 2249-7781

lesionproducedbyaspirin andethanol. Theseinducingmethodsof gastric lesionsarerapid andconvenient wayofscreening plantextractsfor antiulcer potency andcytoprotectionin macroscopically andmicroscopically visible lesions. Diclofenac induced gastric ulcers hasbeen widely used for theexperimentalevaluationof antiulcer activity. Diclofenac induced gastric lesionformation maybeduetostasisin gastric bloodflow,whichcontributesto the development of the hemorrhagic andnecrotic aspectof tissueinjury.Itis ofinteresttonotethatadministrationof antioxidants inhibit aspirin induced gastricinjuryin therats. Canthiumdicoccum possess significant antioxidantactivity. Inconclusion, the antiulcereffectsoftheaboveplantshave been reportedearlier,but there are no studies reporting the combination of these herbals andtheir activityinthese models are quite impressive. The antiulcer activityoftheformulation Canthiumdicoccumcanbecompared to theactivityof thestandarddrug Ranitidine.

IV. SUMMARY & CONCLUSION

Fromtheresultsdiscussedaboveitcan besummarizedthat theFormulationof Canthiumdicoccum possess theantiulcer activityagainsttheDiclofenac sodium induced gastriculcerationanimalmodel ofrats.Atthe dose leveltesteditdoes not show any signs oftoxic effects in treatedmiceaswellasrats.Pepticulcer is the most common disease. Many drugs are there inmarketto treat the ulcer,buttheyarehavinglotof adverse effects.Inthepresent theory,using combination ofherbal drugshasproved that these are the effective alternatives for chemical drugs.The Anti-ulcer Herbal formulation Canthiumdicoccum ishaving significant activity inanimals models used, as compared to the standarddrugRanitidine.

EFFECTOFFORMULATIONONGASTRICVOLUME

Groups	Bodywt. ofrats	Drugsgiven	Gastricvolume
GROUPI	177.2±1.15	Diclofenacsodium +2%Tween80	1±0.04
GROUPII	161.2±2.15	Ranitidine+ Diclofenacsodium	0.8±0.05
GROUPIII	172.5±4.45	Herbalformulation +Diclofenac sodium	0.6±0.03*
GROUPIV	164.4±1.16	Herbalformulation (doubledose)+ Diclofenacsodium	0.5±0.04**

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1351-1359 www.ijprajournal.com ISSN: 2249-7781

Valuesareexpressedinterms ofmean±SEMof5rats(ANOVA)
Pvalues:**<0.001-Highlysignificant *<0.05-SignificantNS:NonSignificant

DosePatternInDiclofenacSodiumInducedUlcerRats

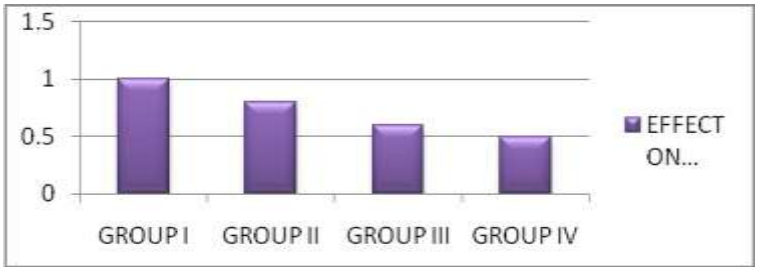
S.NO	Wtofrats(g)	Drugs	Dose(ml)
I)CONTROL GROUP:			
H	177.2±1.15		0.7+0.5
B			0.6+0.5
T_1			0.8+0.5
T_2			0.6+0.5
T_3			0.7+0.5
II)STANDARD GROUP:			
H	161.2±2.15	Diclofenac+ Ranitidine	0.8+0.62
B			0.9+0.67
T_1			0.8+0.63
T_2			0.8+0.64
T_3			0.9+0.65
III)DOSEI:			
H	172.5±4.45	Extract+Diclofenac	0.5+0.64
B			0.6+0.75
T_1			0.5+0.66
T_2			0.5+0.70
T_3			0.6+0.72
IV)DOSEII:			
H	164.4±1.16	Extract(double dose)+diclofenac	1+0.67
B			1+0.65
T_1			1+0.65
T_2			1+0.66
T_3			1+0.68

PHYTOCHEMICALSCREENING

S No.	Test	Pet ether Extract	Chloroform Extract	Methanolic Extract
	Carbohydrates			
1	Mohlish'stest	+ +	+ +	++
	Fehling'stest	+ +	+ +	++
2	Proteins and aminoAcids			

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1351-1359 www.ijprajournal.com ISSN: 2249-7781

	Ninhydrintest	+		+	+
	Biurettest	+		+	+
	Alkaloids				
3	Mayer'stest	++	++		++
	Wagner'stest	++	++		++
	Fixedoilsandfats				
4	Spottest	+	-		-
	Glycosides				
5	Borntrager'stest	+	+		+
	Legalstest	++	+		+
	Triterpenoids				
6	Tin+thionylchloride		+	-	-
	Phenolicsandtannins				
7	Ferricchloridetest	+		+	+
		+		+	+
	Gelatintest	+		+	+
		+		+	+
	Leadacetatetest	+		+	+
		+		+	+
8	Flavonoids	+		+	+



EFFECTOFFORMULATIONONFREEACIDITYANDTOTALACIDITY

Groups	Bodywt.of rats	Drugsgiven	FreeAcidity	TotalAcidity
I	177.2±1.15	Diclofenacsodium +2%Tween80	14.70±0.29	29.6±0.69
II	161.2±2.15	Ranitidine+ Diclofenacsodium	8.8±0.31	15.56±0.69
III	172.5±4.45	Formulation+ Diclofenacsodium	7.3±0.32*	12.56±0.68*
IV	164.4±1.16	Formulation (doubledose)+ Diclofenac	4.6±0.42**	9.5±0.59**

Valuesareexpressedintermsofmean±SEMof5rats(ANOVA)
Pvalues:**<0.001-Highlysignificant
*<0.05-SignificantNS:NonSignificant

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1351-1359 www.ijprajournal.com ISSN: 2249-7781

EFFECTOFFORMULATIONONULCERINDEX

Groups	Bodywtofrats	Drugsgiven	Ulcerindex
GROUPI	177.2±1.15	Diclofenacsodium +2%Tween80	3.7±0.14
GROUPII	161.2±2.15	Ranitidine+Asprin	2.2±0.10
GROUPIII	172.5±4.45	Formulation+ Diclofenacsodium	2±0.18*
GROUPIV	164.4±1.16	Formulation (doubledose)+ Diclofenacsodium	1.5±0.9**

Valuesareexpressedinterms ofmean±SEMof5rats(ANOVA)
Pvalues:*<0.001-Highlysignificant; **<0.05-Significant;NS:NonSignificant

REFERENCES

[1]. TextbookofpathophysiologybyR.K.Marya,year2002,PageNo.52-54.
[2]. Essentials of Medicalpharmacology KDTripathi 4th edition, Year1999, PageNo.629–642.
[3]. Goodman and Gilman's The pharmacological basis of therapeutics11th edition,year2006, PageNo.978-980.
[4]. Pharmacology and pharmacotherapeutics byR.S. Satoskar, SDBhandarkar, S.S. Ainapure Revised20th edition, 2007, PageNo.610–618.
[5]. Clinicalpharmacyand therapeutics.RogerWalkerand CliveEdwards 3rdedition, year 2003,page no.146 –147.
[6]. Drugdiscovery andevaluation–pharmacologicalassayh. Gerhard vogel,wolfgangh.Vog62.
[7]. Arthur guyton c. Text book of medical physiology. 10thed. Harcourt publisherinternational company,singapore;2000:264-379.el.Year1997,pageno.486-491.
[8]. Herfindal,gourley.Text book of therapeutic drug and disease management.7thedn. Charcillivingstone,london;2000:425-36.
[9]. Barrym, brenner,floydc,rector.The kidney6thed. w.b.saunderscompany, philadelphia;2000:3-67.
[10]. Paulmunsonl.principlesof pharmacology,basic concepts and clinical applications. Chapmanandhallitpan international thomson publishingcompany, newyork;685.
[11]. Best,taylors.Physiological basis of medical practice.11thed. Williams andwilkins.London;1984:451-544.
[12]. Goodman,gilman'sThepharmacological basis of therapeutics.10thed.
[13]. Ch.santhoshkumari,Prasad &sreeramuludeterminationofin-vitro&in-vivo activities of aloevera.l againsth.pylori.
[14]. S.Subramanian,D.Sathishkumar,P.Arulselvan,G.P.Senthilkumar&u.smahadevrao,evaluationofantiulcerogenic potential of aloe-vera leaf gel extract studiedin experimentalrats.
[15]. Kossimetowogo,amegnonaagbonon,gastro protective effectof hydroalcoholicextract of aloe burttneri.
[16]. R.Teradaira,N.Shinzato,H.Beppu&K.Fujita, antigastriculcer effects in ratsof

aloearborscensmillervar. Natalensis berger extract.

[17]. Narrayaeomlamnam,suthilukpatumraj&naruemonvisedo pas,effectofaloevera&sucralfateon gastric microcirculatory changes,cytokinelevels,gastriculcerhealing inrats.

[18]. Rafatullah s,tariq m, al-yahja ma, mossaj.s,ageela.m, evaluationof turmeric(curcumalonga)forgastric and duodenal antiulcer activity in rats.J. Ethanopharmacol.1990,29(1):25-34.

[19]. Bhargava KP,SinghN;Evaluation of thegastric antiulceractivity offixed oilofocimumsanctum (holybsil).