RESEARCH PAPER

In Silico Investigation of Wound Healing Potential of Acmella oleracea in Diabetic Foot Ulcers

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ABSTRACT

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia, which often leads to complications such as impaired wound healing, particularly diabetic foot ulcers (DFU). Delayed healing increases the risk of infection due to poor circulation, neuropathy, and reduced immune response. Traditional medicinal plants have gained attention as potential alternatives for managing such complications. Acmella oleracea, a medicinal plant from the Asteraceae family, is widely used in traditional systems for its antimicrobial, anti-inflammatory, immunomodulatory, and wound healing properties. This study aims to investigate the potential of Acmella oleracea in diabetic wound healing using an in-silico network pharmacology approach. Phytochemical data were obtained from the IMPPAT database, identifying key bioactive compounds such as spilanthene, spilanthol, cosmosiin, rutin, and quercetin-3-glucoside. Target prediction was performed using SwissTargetPrediction, while disease-associated genes related to diabetic wounds were collected from DisGeNET. Overlapping targets were identified using Venn diagram analysis, and interaction networks were constructed using Cytoscape. The analysis revealed significant interactions between the plant's bioactives and key molecular targets involved in diabetic wound healing, including MMP1, MMP9, OPRM1, PRKCA, PRKCB, PTPN1, MAPK14, and TNF. These targets are associated with inflammation, tissue remodeling, and cellular signaling pathways critical for wound repair. The findings suggest that Acmella oleracea exhibits multi-target therapeutic potential against diabetic wounds through its bioactive compounds. This study supports the relevance of network pharmacology in validating traditional medicinal plants and highlights Acmella oleracea as a promising candidate for further experimental and clinical research in diabetic wound management.

Keywords: Acemella oleracea, Network Pharmacology, Diabetic wound, IMPPAT, Swiss Target Prediction, Venny, DisGeNET.

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INTRODUCTION:

Diabetes is also associated with poor circulation, which further compounds the problem, because strong circulation is needed for red blood cells to deliver nutrients to the wound. This leads the wound vulnerable to infection and deficient in the nutrients it needs to heal.

Diabetes also causes nerve damage. This means that you might not be able to feel or sense the infected, slow-healing wound on your body.

Diabetic foot ulcer infections are mostly polymicrobial, involving both aerobic and anaerobic bacteria that grow in synergy

Diabetic wound can take longer to heal; diabetes interrupts the body's natural and efficient healing process. The imbalanced blood glucose levels associated with diabetes essentially strangle white blood cells and impair their function. Without WBC to ward off bacteria, infection can effortlessly take root and spread throughout wound.

Nowadays, the major problem of diabetic patients is slow wound healing. Medicinal herbs have some active ingredients play a vital role to heal diabetic wounds (Lalit *et.al*., 2021)

Acemella oleracea is an important medicinal plant belonging to the Asteraceae, commonly known as toothache plant in tamil. It is traditional use in ancient system of medicine for the treatment of toothache, antipyretic,anti-inflammatory, immunomodulatory, hepatoprotective, anticancer, antidiuretic and antioxidant.

Acemella oleracea potent antimicrobial activity against the bacteria and fungus with lowest concentration. The microorganism staypylococus areaus Bassilus stabilanthus, E.Coli, Pseudomonus orgnosacandida alprrica showed a higest zone o inhipition these are the microbes are mostly responsible or diabetic wound infection

Traditional medicines are source of good phytoconstituents which are effective against the targets of various complex diseases. Traditional medicines like Siddha are considered as attractive options in new drug discovery.Many bioactives from traditional medicine sources could serve as good starting compounds and scaffolds for rational drug design. Most of these compounds are part of routinely-used, traditional medicines and hence their tolerance and safety are relatively better known than any other chemical entities that are new for human use (Dewick*et.al*.,2002)

The utility of natural products as sources of novel structures, but not necessarily the final drug entity, is still under practice and the influence of natural product structures is quite marked, with the anti-infective area being dependent on natural products and their structures Recently, a new technique known as poly-pharmacology has emerged. This technique is able to address the limitations with current drug discovery challenges. Poly-pharmacology, also known as network pharmacology, attempts to understand drug action and interactions with multiple targets. A concept of 'network target' has been proposed to help design and predict the best possible treatments (Umachandran,*et.al*., 2015).

A comprehensive online database on the phytochemistry of Indian
medicinal plants will enable computational approaches towards natural product-based drug discovery. IMPPAT, a manually curated database of Indian Medicinal Plants, Phytochemicals, And Therapeutic uses spanning plant-phytochemical associations and plant-therapeutic associations. (Karthikeyan Mohanraj*et.al*., 2016)

The graphic way to represent interactions can be read easily by venn diagrame, it shows all the logical relations and overlaps between the sets. It was widely used in clinical and public health research. (Bulanov *et.al*. 2020)

Cytoscape's software provides basic functionality for the core layout and visually integrate the network with exposure profiles, phenotypes, and other molecular states; (Paul*et.al*.,2003)

The phytoconstituents present in *Acemella oleracea* botanical has been utilized to create pharmacology networks of the formulation using CYTOSCAPE based on the data collected from different databases. The networks represent the interaction of botanicals present in the formulation against the targets of the wound healing and other related diseases.

MATERIALS AND METHODS

Bioactives:

Details of the phytoconstituents (bioactivators) in the plants are obtained from IMPPAT database is a openly accessible at: (*https://cb.imsc.res.in/imppat*.) It will provide the information about Phytochemicals list and also Structure, Physicochemical properties, ADMET, Drug ability scores,Predicted human target proteins, of the phytochemicals (ref)

Targets and Genes:

Target table using SwissTargetPrediction (http://www.swisstargetprediction.ch/).SwissTargetPrediction is an open tool for predicting targets of bioactives in human and other vertebrates.It is useful to understand the molecular mechanisms principle the given bioactivity, to rationalize potential side effects, or to predict the targets of known molecules.

Disease types and indications:

The disease related gene were searched in the DisGeNET platform (http://www.disgenet.org/) and Target of bioactives for their association with any disease or indication. The diseases were clustered into classified disease classes.

Venn Diagram:

A Venn diagram demonstrate the association between two or more sets of data

Venn diagrams are very useful for focus oncorrelation and contrast and are commonly used to compare the characteristics of different data sets.Circles are used to represent each piece of data in a Venn diagram

Network construction

A network is created by constituent of plant, bioactive, associate target and gene related with relevant disease. The networks were constructed using Cytoscape 3.2.0; a java based open-source software. The tools available in Cytoscape were used for analysing the networks. It is a computational method to predict targets for diseases by exploring drug- interactions by implementing a computational platform that integrates the bioactives with the targets and its pathways.

RESULTS AND DISCUSSION

Bioactives:

Details of the bioactis of *Acemella oleracea* in the plans are obtained from IMPPAT database. There are 5 bioactive compounds as present the *Acemella oleracea* which are tabulated. The bioactive compound is Spilanthene, Spilanthol, Cosmosiin, Rutin,

Quercetin-3-glucoside

Plant	Part	Bio actives
Acmella oleracea	Whole plant	Spilanthene
Acmella oleracea	Whole plant	Spilanthol
Acmella oleracea	Aerial part	Cosmosiin
Acmella oleracea	Aerial part	Rutin
Acmella oleracea	Aerial part	Quercetin-3-glucoside

Targets and Genes:

SwissTarget Prediction of bioactives compound in Target and gene tables related to the bioactives of the plant (http://www.swisstargetprediction.ch/).

Spilan thene	Spilanthol	Cosmosii n	Rutin	Querc etin-3-glucos ide
EDNR A	CNR1	TNF	NMUR 2	AKR1 B1
ACE	CNR2	IL2	ADRA 2A	CA2
SLC29 A1	TRPV1	AKR1B1	ADRA 2C	CA7
AKR1 B1	PPARG	ADORA1	ACHE	CA12
F2	PPARA	CA7	AKR1 B1	CA4
PRKC A	PPARD	CA12	NOX4	NOX4
OPRK 1	TRPA1	XDH	CA7	ADRA 2C
MET	OPRM1	RPS6KA 3	CA12	ACHE
ADK	GRM5	ACHE	CA4	NQO2
CA12	CHRM1	NQO2	CA2	RPS6 KA3
CDK2 CCNA 1 CCNA 2	PTGS1	ALDH2	RPS6K A3	NMU R2
MMP1 4	PTGS2	NMUR2	NQO2	ADRA 2A
HCAR 2	MTNR1A	ADRA2A	XDH	PTGS 2
PTPN1	MTNR1B	EGFR	CD38	CD38
PTGF R	EPHX1	CA1	PTGS2	PDE5 A
YARS	ICMT	CD38	PDE5 A	TNF
PYGL	OPRD1	PDE5A	TNF	IL2
ITGB1 ITGA4	HCRTR2	SLC29A1	IL2	ADOR A1
ADA	HCRTR1	CA2	ADOR A1	XDH
MMP7	TRPM8	CA4	ALOX 5	ALOX 5
IGFBP 5	MAPK14	F10	TERT	SLC29 A1
ADRB 3	KCNA5	ABCB1	ADOR A3	TERT
KDM5 B	PTK2	ALOX5	VCP	ADOR A3

BRAF	NQO2	NOX4	SLC29 A1	PLG
TKT	PGR	ADRA2C	TNNC 1 TNNT 2 TNNI3	KCNA 3
SLC5 A2	NAMPT	SIGMAR 1	SQLE	ABCG 2
MAP2 K1	MAPK13	DRD2	PLG	SRC
OPRM 1	HPGD	PRKCG	ABCG 2	APP
SCN9 A	EPHX2	PRKCD	CYP1 B1	F10
BCL2 L1	GRM2	PRKCA	KCNA 3	CYP1 B1
TTL	AVPR1A	PRKCB	TDP1	MCL1
FLT1	CYP19A1	PRKCZ	TP53	ITGA V ITGB3
PTGD R2	HTR2C	PRKCE	ESR1	ITGA V ITGB6
FUCA 1	DRD3	PRKCH	SERPI NE1	KISS1 R
MMP8	OPRK1	PRKACA	PRKC G	ITGA2 B ITGB3
OGA	PDE10A	CA13	PRKC D	ITGB1 ITGA5
CA14	CHRM2	KDM5A	PRKC A	ALDH 2
ADOR A2A	CSF1R	CA9	PRKC B	CA1
EGFR	PSEN2 PSENEN NCSTN APH1A PSEN1 APH1B	PLG	PRKC Z	CA13
ECE1	LCK	ADORA3	PRKC E	CHEK 2
HSP90 AB1	KDR	ADORA2 A	PRKC H	PRKC G
KDM3 A	SIGMAR1	ITGAV ITGB3	PRKA CA	PRKC D
CXCR 2	P2RX7	PTGS2	APP	PRKC A
KDM4 D	HTR6	CYP1B1	F10	PRKC B
KIT	PABPC1	ABCG2	KISS1 R	PRKC E
EPHX 2	CMA1	TP53	MCL1	PRKC H
MAPK 10	TAOK1	KISS1R	CHEK 2	CHEK 1
HK2	TAOK3	PIM1	CHEK 1	RAF1
HK1	HSD11B1	SQLE	ALDH 2	HSP90 AB1
FABP4	NR3C1	KIT	HSP90 AB1	ADOR A2A
MMP1	GABRB3 GABRA3	OPRD1	KCNH 2	PIK3C A

	GABRG2			
AKR1 C3	GABRB3 GABRG2 GABRA1	ABCC1	CCR1	IKBK B
TOP1	GABRA2 GABRB3 GABRG2	KCNA3	CA1	DNM2
AGTR 1	CXCR2	F7	CA9	CDK1 CCNB 1
IGFBP 3	MTOR	TNKS2	CA13	PRKC Z
CA2	PARP1	TNKS	EGFR	PRKA CA
ADOR A3	PIK3CA	TNNC1 TNNT2 TNNI3	ADOR A2A	MAPT
PIM1	GPBAR1	FLT3	MAPT	KDM4 E
PYGM	CRHR1	MAOA	KDM4 E	GPR3 5
CA1	PANK3	CCNB3 CDK1 CCNB1 CCNB2	GPR35	AVPR 2
DHOD H	FASN	CDK6	AVPR 2	TOP2 A
LTA4 H	BAZ2B	SYK	TOP2 A	MAO A
HRAS	CHRM4	GSK3B	MAO A	IGF1R
JAK3	CHRM5	HSD17B 1	IGF1R	FLT3
RAF1	DRD2	TTR	FLT3	CYP1 9A1
KDM4 C	DRD4	CSNK2A 1	CYP19 A1	INSR
MMP1 3	CHRM3	CFTR	INSR	EGFR
AMPD 3	BAZ2A	AKR1B1 0	F2	PIM1
MAPK 8	CTSB	PTPRS	PIM1	AURK B
SLC5 A1	NPY5R	AMY1A	AURK B	DRD4
TYR	NR3C2	ITGAV ITGB6	DRD4	GLO1
MME	CTSS	PLA2G2 A	GLO1	MYL K
SELE	PTGER1	ITGA2B ITGB3	MYLK	MPO
MKN K2	SLC6A9	ITGB1 ITGA5	MPO	PIK3R 1
CA9	TSPO	OPRM1	PIK3R 1	DAPK 1
MGA M	OXTR	GLO1	DAPK 1	PYGL
SI	MAPKAPK2	APP	PYGL	SYK
ERN1	CYP11B2	PARP1	SYK	GSK3 B
PPP2C A	PSMB5	MMP9	GSK3 B	PTK2
PRKC	SMO	MMP2	PTK2	HSD1

B				7B2
ELAVL1	HDAC6	MMP12	HSD17B2	KDR
PTPRG	DYRK1A	ARG1	KDR	MMP13
GLRA2	HDAC1	SERPINE1	MMP13	MMP3
PLA2G1B	MCHR1	CYP1A1	MMP3	CA3
HSD11B2	P2RY12	CYP1A2	CA3	ALOX15
ATP2A1	RPS6KA3	TERT	ALOX15	PLK1
PRKCE	CTSV	F9	PLK1	CDK1
PPP1CC	PTPN1	NQO1	CA6	MMP9
RORC	CTSL	PTGES	CDK1	PIK3CG
CXCR1	RORC	AR	MMP9	MMP2
ATP1A1	FLT1	CBR1	PIK3CG	PKN1
GLI1	JAK3	KDM4E	MMP2	CA14
PRKCQ	JAK1	ALOX15	PKN1	CSNK2A1
PTAFR	BRD4	CDK1	CA14	ALOX12
GLRA1	BRD2	ALOX12	CSNK2A1	MET
PRKCH	BRD3	ODC1	ALOX12	NEK2
PPM1B	MAOA	ABL1	MET	CXCR1
PPP2R5A	MAOB	NAE1	NEK2	CAMK2B
GSTM1	CREBBP	PFKFB3	CXCR1	ALK
IL2	CYP11B1	SLC5A2	CAMK2B	AKT1

Disease types and indications:

The disease related gene were searched in the DisGeNET platform (http://www.disgenet.org/) and Target of bioactives for their association with any disease or indication. The diseases were clustered into classified disease classes.

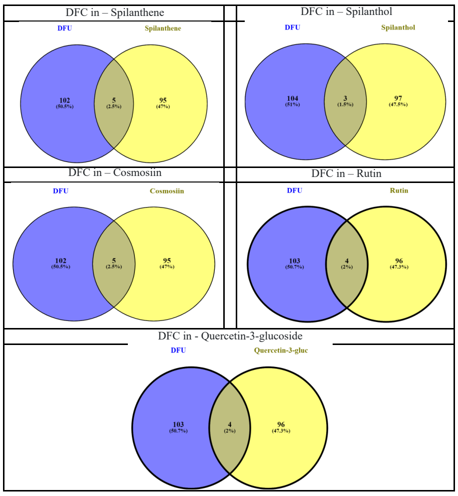
Gene Associate with Diabetic Foot Wound			
DEFB4B	CXCL8	ASAH2	CD248
MIR23C	ITGAM	CD248	HNP1
ABCB6	LEP	HNP1	PTH
TUBB4B	SMIM10L2A	PTH	PTPN1
SLC9A6	LOX	PTPN1	RPS20
TNFSF13B	MIR126	RPS20	S100A8
IL24	MIR145	S100A8	SAG
PRRT2	MIR155	SAG	CCL2
CRP	MIR15B	CCL2	CXCL6
DEFB104A	MIR203A	CXCL6	CXCL5
MAPK14	MIR21	CXCL5	CXCL12
CCN2	MIR217	CXCL12	POU5F1P3
GADD45A	MIR23A	POU5F1P3	SMIM10L2B
DEFA3	MIR23B	SMIM10L2B	POU5F1P4
DEFB4A	IR34A	POU5F1P4	SPP1
DIH1	MMP1	SPP1	ADAM17
AGER	MMP9	ADAM17	TCF7L2
AGT	MMP10	TCF7L2	BTK
EGF	NEUROD1	BTK	PRDX2
ELN	NFE2L2	PRDX2	TEK
GABPA	CCN3	TEK	TGFB1
GJA1	NTS	TGFB1	TIMP1
IL17B	OPRM1	TIMP1	TIMP2
PDCD4	OXA1L	TIMP2	TIMP3
ANG	DEFB104B	TIMP3	TLR4
LINC00641	IL20	TLR4	TNF
ANGPT2	PDGFB	TNF	C4BPA
LINC00692	PGF	C4BPA	VDR
HDAC2	POU5F1	PRKCA	VEGFA
HIF1A	PRKCA	PRKCB	VIP
HSPA4	PRKCB	MAPK1	CARD14
HSPB1	MAPK1	MAP2K7	NANOG
HSPB2	MAP2K7	PRNP	CAMP
IL6	PRNP	ASAH2	SERPINH1
NOS1AP	CD33	EOLA1	HSPB3

Venn diagram:

A Venn diagram Represent the association between gene related to diabetic foot ulcer and gene related to bioactives in plant.

DFC in - Spilanthene	DFC in – Spilanthol	DFC in - Cosmosiin	DFC in - Rutin	DFC in - Quercetin-3-glucoside
MMP1	MAPK	MMP9	MMP	MMP9

	14		9	
OPRM1	OPRM 1	OPRM 1	PRK CA	PRKC A
PRKCA	PTPN1	PRKC A	PRK CB	PRKC B
PRKCB		PRKC B	TNF	TNF
PTPN1		TNF		
Gene Assosicieted with DFC Gene				
MMP1, OPRM1, PRKCA, PRKCB PTPN1, MAPK14, MMP9, TNF				



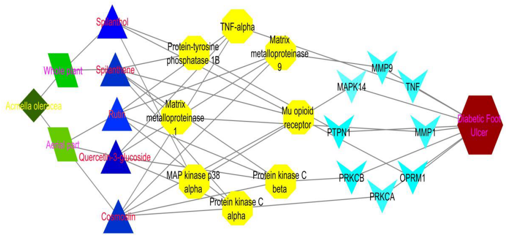
NETWORK CONSTRUCTION

A network is formed by constituent of plant, bioactive, Associate Target and Gene related with relevant disease. The networks were constructed using Cytoscape 3.2.0; a java based open-source software.

***Acmella oleracea* - Diabetic Foot Ulcer Network Table**

Plant	Part	ABI	Target	Gene	Disease -Diabetic Foot Ulcer
Acmella oleracea	Whole plant	Spilanthene	Matrix metalloproteinase 1	MMP1	DFU
Acmella oleracea	Whole plant	Spilanthene	Mu opioid receptor	OPRM1	DFU
Acmella oleracea	Whole plant	Spilanthene	Protein kinase C alpha	PRKCA	DFU
Acmella oleracea	Whole plant	Spilanthene	Protein kinase C beta	PRKCB	DFU
Acmella oleracea	Whole plant	Spilanthene	Protein-tyrosine phosphatase 1B	PTPN1	DFU
Acmella oleracea	Whole plant	Spilanthol	MAP kinase p38 alpha	MAPK14	DFU
Acmella oleracea	Whole plant	Spilanthol	Mu Opioid receptor	OPRM1	DFU
Acmella oleracea	Whole plant	Spilanthol	Protein-tyrosine phosphatase 1B	PTPN1	DFU
Acmella oleracea	Aerial part	Cosmosiin	Matrix metalloproteinase 9	MMP9	DFU
Acmella oleracea	Aerial part	Cosmosiin	Mu opioid receptor	OPRM1	DFU
Acmella oleracea	Aerial part	Cosmosiin	Protein kinase C alpha	PRKCA	DFU
Acmella oleracea	Aerial part	Cosmosiin	Protein kinase C beta	PRKCB	DFU
Acmella oleracea	Aerial part	Cosmosiin	TNF-alpha	TNF	DFU
Acmella oleracea	Aerial part	Rutin	Matrix metalloproteinase 9	MMP9	DFU
Acmella oleracea	Aerial part	Rutin	Protein kinase C alpha	PRKCA	DFU
Acmella oleracea	Aerial part	Rutin	Protein kinase C beta	PRKCB	DFU
Acmella oleracea	Aerial part	Rutin	TNF-alpha	TNF	DFU
Acmella oleracea	Aerial part	Quercetin-3-glucoside	Matrix metalloproteinase 9	MMP9	DFU
Acmella oleracea	Aerial part	Quercetin-3-glucoside	Protein kinase C alpha	PRKCA	DFU
Acmella oleracea	Aerial part	Quercetin-3-glucoside	Protein kinase C beta	PRKCB	DFU
Acmella oleracea	Aerial part	Quercetin-3-glucoside	TNF-alpha	TNF	DFU

***Acmella oleracea* - Diabetic Foot Ulcer Network Table**



DISCUSSION

In general, science has all the wonderful advances in synthetic chemistry. Unfortunately, it does not help to alleviate and cure all the diseases in the world. According to studies scientific medicine in developing countries serves only a minority while the 30 to 50 % of the population supports their health through traditional medicine. A positive aspect of medicinal plants is their low cost compared to the high cost of new synthetic drugs. It has become completely inaccessible to the majority of people (Chaudhari et.al, 2018).

Herbal compounds have strong antimicrobial activity against microorganisms that are isolated from diabetic wounds or applied to infected diabetic wounds, Herbal preparations can be used as an alternative to synthetic drugs for conventional treatment of diabetic wounds. (Herman et.al., 2023)

Acemella oleracea has been traditionally used for many disease, it's famous as a folklore remedy for toothache and for throat infections (Chung et.al, 2008). also known to be used as panacea (Sumatra), as stimulant, for toothache (Sudan), for stomatitis (Java), and for wound healing (India) (Hossan et.al 2010). The whole plant paste used as "poisonoussting" in Chittagong hill tracts of Bangladesh where the plant is also known as Jhummosak (Biswas et.al 2010). In Cameroon, the plant is used as a snake bite remedy and in the treatment of articular rheumatism (Santesson et.al 1926). It is traditional use in ancient system of medicinefor the treatment of toothache, antipyretic,anti-inflammatory, immunomodulatory, hepatoprotective, anticancer, antidiuretic and antioxidant. (Sabitha et.al., 2019)

Same vitro studies show moderate effect on antioxidant activity, cytotoxicity evaluation, thrombolytic activities and antimicrobial activity against gram-negative. and gram-positive microorganisms. (Mahbubol et.al,2023) Acmella oleracea traditionally used in many systems of medicine for the treatment of infection, diuretics, antimalarial, antibacterial, antiulcer, immunomodulatory, anashthetic, antifungal, insecticide, etc. It also heals wounds because anti fungal and anti bacterial nature. (Priti et. al. 2022). Film made by Jambu evaluated anesthetic action and wound healing activity through in vivo tests. And histopathological analysis emonstrated that it increases collagen synthesis and epidermal thickening. The results demonstrate that the films have potential application in the treatment of skin wounds, pressure ulcers and infected surgical wounds (Lais et.al., 2016)

The roots and all aerial parts of the plant contain biochemical components such as spilanthol, alkamide, spilanthol, scopoletin, myricene, amyrin, amyrin. Spilanthol has high industrial demand for its use in pharmaceutical, cosmetic and toothpaste industries. Due to its wide applications for commercial use, S.acmella is rapidly declining from its natural habitat.(Sabitha et.al., 2019)

Summary of in vitro and in vivo experimental reports on the activities of S. acmella, how they contributed potential health benefits in reducing the risk of diseases associated with oxidative stress, inflammatory targets such as inducible nitric oxide synthase (iNOS), nuclear factor-κB family of transcription factors (NF-κB), cyclooxygenase-2 (COX-2) and nitrogen-activated protein kinase (MAPK). (Abdul et.al 2021)

An insilico library provide information of phytochemicals structure and also ADMET (absorption, distribution, metabolism, excretion, toxicity) and drug-likeliness properties (Karthikeyan et. al., 2018)

Venn diagrams are widely used in clinical and public health research Statements that represent logical relationships between Two or more data sets. (Nikolay et.al., 2020)

The results of silico analysis revealed that the bioactives in the plant are capable of working against key targets of diabetic Foot ulcer, such as MMP9, OPRM1, RKCA, PRKCB, TNF, etc.

Computational approach called network pharmacology has been used to explore the potential applications of the Phyto chemicals present in the plant. It provides hypothetical idea about the action of plants against the specific targets. The network of interactions between natural products and target proteins helps to find out potential drug leads and novel interactions leading to the multi gene-multi target, discovery approach. The results indicate that the botanical is found to possess Diabetic wound healing property

CONCLUSION:

Acmella oleracea has significant potential in the treatment of diabetic wounds due to its antimicrobial, anti-inflammatory, antioxidant, and wound healing properties. Its traditional use is supported by in vitro and in vivo studies indicating enhanced collagen synthesis and tissue regeneration. Biologically active compounds such as spilanthol contribute to its pharmacological effects, while computational and network pharmacology analyses indicate multi-target interactions with key proteins involved in diabetic ulcer pathology. Despite these promising findings, current evidence is largely preclinical. Further clinical studies, along with standardization and safety assessments, are needed to confirm its therapeutic utility. Overall, Acmeella oleracea offers a promising, cost-effective natural approach to healing diabetic ulcers; future research is needed to support its clinical use and sustainable development.

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