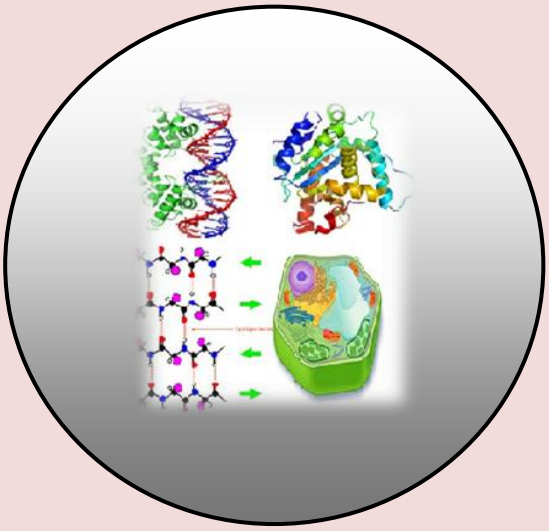
Anti-inflammatory Properties of some Active Components obtained from Plants

By
Debjani Sarkar

ISSN 2319-3077 Online/Electronic
ISSN 0970-4973 Print

UGC Approved Journal No. 62923
MCI Validated Journal
Index Copernicus International Value
IC Value of Journal 82.43 Poland, Europe (2016)
Journal Impact Factor: 4.275
Global Impact factor of Journal: 0.876
Scientific Journals Impact Factor: 3.285
InfoBase Impact Factor: 3.66

J. Biol. Chem. Research
Volume 36 (1) 2019 Pages No. 131-138



Journal of Biological and Chemical Research

An International Peer Reviewed / Referred Journal of Life Sciences and Chemistry

Indexed, Abstracted and Cited in various International and National Scientific Databases

Published by Society for Advancement of Sciences®

J. Biol. Chem. Research. Vol. 36, No. 1: 131-138, 2019
(An International Peer Reviewed / Refereed Journal of Life Sciences and Chemistry)
Ms 36/02/01/2019

ISSN 2319-3077 (Online/Electronic)
ISSN 0970-4973 (Print)

Debjani Sarkar
http:// www.sasjournals.com
http:// www.jbcr.co.in
jbiolchemres@gmail.com

RESEARCH PAPER
Received: 21/04/2019 Revised: 11/05/2019 Accepted: 12/05/2019

Anti-inflammatory Properties of some Active Components obtained from Plants

Debjani Sarkar

Department of Zoology, A.P.C. Roy Govt. College, Himanchal Vihar, Matigara, Siliguri, Darjeeling -734010, West Bengal, India

ABSTRACT

Plant derived products are cheap with almost no side effects and therefore can serve as a better alternative to treat inflammation instead of the oral synthetic drugs available in the market. A great number of plants/plant parts showing anti-inflammatory activity have been studied and their active components have been identified. The present review focuses on the different active components obtained from various plants showing anti-inflammatory activity and their mechanism of action.
Keywords: Inflammation, Plant-Derived Products, Active Components and Mechanism of Action.

INTRODUCTION

Inflammation is defined as the reaction that occurs when the body is attacked by an infectious mediator, challenged by an antigen or suffers any form of damage (Goldsby *et al*., 2003). The inflammation developed, in most cases, is healed naturally but if the load of antigen is heavy or if it is found at an abnormal location it may lead to visible inflammation requiring treatment.

The initiation of inflammatory response is seen as blanching of skin caused by temporary vasoconstriction. This is followed by:

1. The acute vascular response or "wheal and flare reactions" resulting from vasodilatation and increased capillary permeability which leads to increased blood flow (hyperaemia) causing erythema and oedema (Roitt *et al*., 2001).
2. If the tissue damage is adequate, the acute cellular response occurs over the next few hours, characterized by infiltration of neutrophils, into the damaged area by margination (attachment with endothelial cells) and diapedesis.
3. In case of a more severe damage, a chronic cellular response may follow characterized by appearance of macrophages and lymphocytes responsible for microbial killing, in clearing up of debris and in restoring tissues.
4. Resolution occurs in the next few weeks where blood clots are removed and original tissue architecture is restored. Scarring is seen if the tissue is unable to return to its original form. If the infectious particle or accumulated debris are removed partially, a granuloma may be formed.

Mediators of inflammation: The mediators of inflammation include mainly the white blood cells like neutrophils, macrophages etc. The other mediators constitute vasoactive and peptides, derivative of arachidonic acid, reactive oxygen species, cytokines etc.

Arachidonic acid, released from membranes of cells after damage, activates the cycloxygenase and lipoxygenase pathway. Kinins, neuropeptides, histamine, complement component, free radicals and cytokines are also released at the site of tissue injury. The interaction of arachidonic acid with these components results in the perpetuation of the inflammatory process. Inducible nitric oxide synthase (iNOS) catalyzes the formation of nitric oxide (NO), (Andrew and Mayer, 1999), which in turn activates cycloxygenase (COX), that converts arachidonic acid to prostaglandins (Wang *et al*., 2007) responsible for inflammatory response. The secretion of pro-inflammatory cytokines such as IL-1β, IL-6, IL-12, TNF-α etc. are increased and the anti-inflammatory cytokines like IL-10, IL-4 etc. are decreased (Ma & Pope, 2005). The generation of reactive oxygen species (ROS) is also reported to increase during inflammation (Chan, 1999). This is accompanied by decrease of enzymes like catalase, superoxide dismutase (SOD) and non-enzymatic glutathione (GSH) (Sies, 1993). Many signaling pathways are involved in inflammation, the major pathways being nulclear factor- kappa beta (NF-κB) and mitogen activated protein (MAP) kinase pathways which are usually upregulated (Baldwin, 1996). p38 MAP kinase (p38), extracellular signal-regulated kinases 1/2 (ERK1/2) and c-jun N-terminal kinase (JNK) (Garrington and Thompson, 1999; Ruland and Mak, 2003) are the three main MAP kinase pathways studied. Nuclear factor erythroid -2 (Nrf-2) pathway is also involved in inflammation and is usually downregulated (Ahmed *et al*., 2017).

Drawbacks of Current anti-inflammatory drugs: The drugs used currently for treatment of inflammation include the non-steroidal anti-inflammatory drugs (NSAIDs), steroids and disease modifying anti rheumatic drugs (DMARDs) (Payan & Katzung, 1995). The NSAIDs results in relief of pain by inhibiting cycloxygenases, the steroids by slowing down new bone erosions and DMARDs by inhibiting the mediators of inflammation stated above. All of the drugs under these three broad categories are associated with numerous side effects including kidney and heart diseases besides minor symptoms like dizziness, vomiting, headache etc.

Plant products as alternate anti-inflammatory drugs: As the available drugs are associated with various side effects, the search for less toxic yet equally efficacious compounds sourced from nature is an area of intense research (Mckellar *et al*., 2007). India being a mega diversity country possesses a wide variety of medicinal plants, well documented in ancient Indian literature, with a huge possibility for drug development. Plant-derived products are cheap, available in plenty and have very minimum side effects making them a fascinating option.

MATERIAL AND METHODS

The names of the plants having anti-inflammatory properties were identified from various books on medicinal plants and also searched in online database. The active components responsible for the anti-inflammatory activity of plants were then searched in Pubmed, Google, Science Direct etc and their mechanism of action studied. The information accumulated was then presented in a table format.

RESULTS AND DISCUSSION

Active ingredients obtained from plants and their mechanism of action

Phenols obtained from plants are mainly responsible for the inflammatory properties of plants. Phenolic compounds are grouped into flavonoids and non-flavonoids, of which (Bravo, 1998) flavonoids possess significant anti-inflammatory activity (Handa *et al*., 1992). Quercitin, luteolin, acacetin etc. are all naturally occurring flavonoids having anti-inflammatory activity (Table 1). Quercetin is found in green tea, onions, berries, apples, *Ginkgo biloba*, buckwheat tea etc. Luteolin is found in thyme, celery, green peppers, and chamomile tea while acacetin is found in black locust, silver birch and in the fern *Asplenium normale*. All the three flavonoids were responsible for downregulation of inflammation by inhibiting the known mediators of inflammation like NO, iNOS, COX-2, prostaglandins etc. NF- κB and MAP kinase pathways were responsible for the downregulation of the pro-inflammatory cytokines and the other mediators of inflammation. Apocynin, also known as acetovanillone, is found in Canadian hemp, *Picrorhiza kurroa*, etc. Berberine is a benzylisoquinoline alkaloid found in plants of *Berberis* sp. (Oregon, Barberry), Goldenseal and Chinese Goldthread. Coumarin, belonging to benzopyrene group, is an aromatic compound found in tonka bean, vanilla grass, sweet grass etc.

Oleanolic acid, a pentacyclic triterpenoid, is found in *Tripterygium wilfordii* hook and the leaves and fruits of olive tree. Resveratrol is a stilbenoid present in the skin of grapes, blueberries, mulberries, and peanuts. All the above mentioned natural components are potent anti-inflammatory mediators (Table 1). The animals generally used as models of inflammation belonged to various strains of rat (Sprague Dawley, Wistar etc) and mice (ICR, C57BL/6 etc). Inflammation was induced by use of phlogistic agents like lipopolysaccharide (LPS). The body parts used for measuring the various parameters of inflammation included plasma, tissues from different organs, and cells. For *in vitro* studies, mouse peritoneal cells or cell lines were used. RAW264.7 is the general choice for study of the anti-inflammatory activity of the plant product (other cell lines like ICME, HaCaT, HT-29 etc. were also used); the specific cell types were chosen for studying the anti-inflammatory effect related to a particular organ or a particular disorder (Table 1).

Table 1. Active ingredients obtained from various plants and their mode of action.

Plant derived product	**Test System (s)**	**Dose**	**Molecular mechanism(s) of action**	**Reference**
Acacetin	Sprague Dawley rat: Improved the impaired heart function induced by myocardial ischemia/reperfusion injury	10 mg/kg b.w. 250 µg/kg /min 0.3- 3 µM	Decreased Ischemia/reperfusion injury induced TLR4, IL-6 and TNF-α Increased SOD	Liu *et al*., 2016
	Mice: Attenuated sepsis induced lung injury and edema RAW264.7 cells	20-80 mg/kg b.w. 10-100 µg/ml	Decreased sepsis induced myeloperoxidase and neutrophil infiltration, iNOS, COX-2 and PGE2 production Inhibited TNF- α, IL-1 β, IL-6, and MIP-2 Decreased ROS production and increased SOD , GPx and HO-1 activity Inhibited NF-κB activity	Sun *et al*., 2017
	BALB/c mice: Reduced LPS induced inflammation and edema pulmonary micro-vascular endothelial cells (PMVECs)	50 mg/kg b.w. 50 µM	Inhibited LPS induced ROS, TNF- α and IL-1 β Increased HO-1 and Nrf2 activity	Wu *et al*., 2018
Apocynin	RAW 264.7 cells	100-500 µM	Inhibited LPS induced NO, PGE2, TNF- α and IL-1 β Inhibited iNOS and COX-2 expression Inhibited NF-κB, p-38, ERK and JNK activity	Hwang *et al*., 2016
	ICR mice	2.5 mg/kg b.w.	Attenuated ischemia/reperfusion-induced NOX2, NOX4 and ROS Inhibited NLRP3 ASC, caspase-1, IL-1β and IL-18 proteins Inhibited iNOS, COX-2 and NF-κB activation	Qin *et al*., 2017
	Wistar rats: Attenuated	0.5 g drug in	Inhibited carrageenin	Anter *et al*.,

	paw edema and skin irritaion	medicated film	induced COX-2 and NF-κB	2018
Berberine	C57BL/6 mice: Inhibited pancreatic injury and pancreatitis associated lung injury	1 -20 mg/kg b.w.	Inhibited cerulean induced NO and iNOS, TNF- α, IL-1β and IL-6 Inhibited NF-κB , p38 , ERK and JNK activity	Choi *et al*., 2016
	C57BL/6 mice: inhibited colitis-associated tumorigenesis and colonic epithelium hyperproliferation RAW264.7 cells/ICME cell line	1 mg/ml 25 µM	Inhibited LPS induced IL-6 and TNF-α Inhibited EGFR/ERK signalling	Li *et al*., 2017
	HaCaT keratinocytes and HaCaT/THP-1 co-cultures	10-50 µM	Inhibited sulphur mustard induced necrosis and apoptosis Inhibited IL-6 and IL-8	Lang *et al*., 2018
Coumarin	RAW264.7 cells	25-200 µg/ml	Inhibited LPS induced NO production and iNOS mRNA expression	Wang *et al*., 2016
	RAW264.7 cells	10 – 50 µM	Inhibited LPS induced NO, PGE2, TNF-α, NO, IL-6, and IL-1β	Sandhiutami *et al*., 2017
	Rat: Inhibited carrageenin induced paw edema and pathological changes RAW264.7 cells	45 mg/kg b.w. 2.5- 20 µM	Inhibited LPS induced NO, IL-6 and TNF-α Inhibited iNOS, COX-2 expression Inhibited NF-κB and p38 MAP kinase pathways	Chen *et al*., 2017
Luteolin	RAW264.7 cells	0.5 – 5 µM	Inhibited LPS induced NO and iNOS levels Inhibited NF-κB activity Increased HO-1 levels	Sung & Lee, 2015
	ICR mice: Inhibited cerulean and LPS induced pathological scores	25-100 mg/kg b.w.	Inhibited LPS and cerulean induced amylase and lipase activity, TNFα and IL-6 Increased HO-1 and IL-10 Inhibited NF-κB activity	Xiong *et al*., 2017
	HT-29 colon epithelial cells	50-100 µM	Inhibited cytokine induced NO, IL-8, iNOS and COX-2 Inhibited JAK/STAT pathway	Nunes *et al*., 2017
Oleanolic acid	Wistar rats: Inhibited Ischemia/reperfusion (I/R) induced renal damage	12.5 – 50 mg/kg b.w.	Decreased I/R induced blood urea nitrogen, creatinine, kidney injury molecule-1 and lactate dehydrogenase Decreased methane dicarboxylic aldehyde and increased GSH, SOD, catalase and GPx levels Reduced MPO, IFN- γ, IL-6 and increased IL-10 Inhibited Nrf2 and	Long *et al*., 2016

			γ-glutamylcysteine ligase (GCLc) mRNA expression	
	SW982 cells	5 – 20 µM/L	Inhibited IL-1β stimulated IL-6, IL-8 and MMP-1 Inhibited NF-κB, PI3K/Akt, p38 , ERK and JNK activity.	Lian *et al*., 2016
	C57BL/6J and db/db mice chondrocytes	10-50 µM	Inhibited glucose induced PGE2, MMP-13 and IL-6 Increased expression of PPARγ and SOD2	Kang *et al*., 2017
Quercetin	RAW264.7 cells	6.25 – 50 µM	Inhibited LPS induced NO, iNOS and COX-2 and PGE2 Reduced levels of TNF-α, IL-6 and IL-1β Inhibited p38, ERK and JNK pathways	Cho *et al*., 2016
	ICR mice: Inhibited LPS induced paw inflammation RAW264.7 cells	1 and 2 µM/kg b.w. 5-30 µM	Inhibited NO, iNOS , COX-2 and PGE2 Reduced IL-1, IL-6, IFN-γ, TNF- α, IL-3, IL-9, IL-13, GM-CSF, eotaxin, IL-17, G-CSF, and MCP-1 Inhibited SEK1-JNK1/2 and MEK1-ERK1/2	Hisanaga *et a*l., 2016
	BALB/c mice: Inhibited imiquimod induced PASI scores, decrease the temperature of the psoriasis-like lesions, and deteriorating histopathology	3-120 mg/kg b.w.	Inhibited imiquimod induced TNF-α, IL-6 and IL-17 Increased GSH, catalase and SOD Inhibited RelB, TRAF-3 and NF-κB expression	Chen *et al*., 2017
Resveratrol	RAW 264.7 cells	1-40 µM	Downregulated LIPS induced NO, iNOS, IL-6 Inhibited translocation of high-mobility group box 1 (HMGB1), NF-κB from cytoplasm to nucleus Inhibited phosphorylation of STAT 1and 3	Ma *et al*., 2015
	HUVEC s	5-100 µM	Attenuated the TNF-α-induced ICAM-1 expression Inhibited NF-κB and p38 MAPK activity Induced the AMPK phosphorylation and the SIRT1 expression, miR-221/-222 expression	Liu *et al*., 2017
	Human coronary arterial endothelial cells (HCAECs)	10- 100 µM	Inhibited TNF-α-induced ICAM-1, iNOS and IL-1β mRNA	Huang *et al*., 2017

Abbreviations used

AMPK: AMP activated protein kinase, ASC: Apoptosis associated speck like protein, COX-2: cycloxygenase2, EGFR: Epidermal growth factor receptor, Egr: early growth response proteins, ERK: extracellular signal regulated kinase, GCLc: γ-glutamylcysteine ligase, GMCSF: granulocyte macrophage colony stimulating factor, GPX: glutathione peroxidase, GSH: glutathione, HMGB1: high-mobility group box 1, HO: heam oxygenase, ICAM: intercellular adhesion molecule, IFN: interferon, IL: interleukin, iNOS: inducible nitric oxide synthase, JAK: Janus kinase inhibitor, JNK: Jun N terminal kinase, LPS: lipopolysaccharide, MAPK/MEK: mitogen activated protein kinase, MCP: monocyte chemoattractant protein, MDA: malondialdehyde, MIP: macrophage inflammatory protein, MMP: matrix metalloproteinase, NF- κB: Nuclear factor kappa B, NLRP: Leucine rich Repeat and Pyrin domain containing, NO: nitric oxide, NOX: NADPH oxidase, Nrf: nuclear factor (erythroid derived),PASI: Psoriasis area severity index, PGE2: Prostaglandin E2, PI3k: phosphatidylinositol 3-kinase, ROS: Reactive oxygen species, SEK: stress and extracellular-activated kinase, SIRT1: sirtuin, SOD: superoxide dismutase, STAT: signal transducer and activator of transcription, TLR: toll like receptor, TNF: tumor necrosis factor, TRAF: Tumor necrosis factor receptor–associated factor.

The anti-inflammatory property of many of the active plant components was exhibited by their ability to bring down NO, iNOS, chemokines like MCP-1 and pro-inflammatory cytokines like TNF-α, IL-1β, IL-6, IL-8, etc. Upregulation of anti-inflammatory cytokine like IL-10 is also mediated by some active components of plants. The chosen targets of the current anti-inflammatory drugs, cycloxygenase-2 (COX-2) and prostaglandins were also downregulated by majority of compounds derived from plants. Reduction in ROS, lipid peroxidation along with upregulation of the enzymatic (superoxide dismutase, catalase etc) and non-enzymatic (glutathione etc) defense systems were also tested as markers of anti-inflammatory activity. All the above mentioned events were mainly attributed to the downregulation of signaling pathways like NF- κB pathway by the naturally derived plant products. The MAP kinase pathway (p38, ERK and JNK pathway) was also inhibited and Nrf2 pathway activated to bring about a remission of inflammation. In case of some heart, lung or renal disorders, modifications of the inflammatory parameters stated above were useful for arrest of the symptoms (Table 1).

Future Perspectives

The existing anti-inflammatory drugs being associated with various side effects, it is essential to develop new drugs, which are cheap, equally effective but with negligible side effects. In recent times, considerable attention has been focused towards identifying the active component(s) of these traditional preparations. This approach will help in identifying compounds that show specific bioactivity. Therefore, purified plant products either by itself or in combination with standard anti-inflammatory drugs are worthy of future consideration and it is equally important to understand their detailed mechanism of action for their better functioning.

CONCLUSIONS

The pro-inflammatory mediators must be downregulated for the treatment of inflammation along with the upregulation of anti-inflammatory mediators without hampering the normal functions of the body. As the available drugs are yet to be perfected, investigators are researching with the traditional and widely accepted folk medicine in the quest for devising a more improved drug. The present study focuses on the role of the phytoconstituents obtained from plants in reducing inflammation. Most of the plants products exert their effect by reducing the known mediators of inflammation such as NO, TNF-α, IL-6, ROS, COX-2 and prostaglandins. These reductions were due to the inhibition of the signaling pathways like NF-κB pathway or MAP kinase pathways.

ACKNOWLEDGEMENTS

I hereby acknowledge my Ph.D. guide, IPGME&R, for introducing me to the field of medicinal plants with anti-inflammatory properties. I also acknowledge Officer in charge, Acharya Prafulla Chandra Roy Govt. College, and my departmental colleagues for giving me support to carry on my work.

REFERENCES

Ahmed, S.M., Luo, L., Namani, A., Wang, X.J. and Tang, X. (2017). Nrf2 signaling pathway: Pivotal roles in inflammation. *Biochim Biophys Acta Mol Basis Dis.* 1863:585-597.

Andrew, P.J. and Mayer, B. (1999). Enzymatic function of nitric oxide synthases. *Cardiovasc. Res.* 43: 521-531.

Anter, H.M., Hashim, A. II, Awadin, W. and Meshali, M.M. (2018). Novel anti-inflammatory film as a delivery system for the external medication with bioactive phytochemical "Apocynin". *Drug Des. Devel. Ther.* 12: 2981-3001.

Baldwin Jr., A.S. (1996). The NF- kappa B and I kappa B proteins new discoveries and insights. *Annu. Rev. Immunol.* 14: 649-683.

Bravo, L. (1998). Polyphenols: Chemistry, dietary sources, metabolism and nutritional significance. *Nutr. Rev.* 56: 317-333.

Chan, A.C., Chow, C.K. and Chiu, D. (1999). Interaction of antioxidants and their implication in genetic anemia. *Proc. Soc. Exp. Biol. Med.* 222: 274-282.

Chen, H., Lu, C., Liu, H., Wang, M., Zhao, H., Yan, Y. and Han, L. (2017). Quercetin ameliorates imiquimod-induced psoriasis-like skin inflammation in mice via the NF-κB pathway. *Int. Immunopharmacol.* 48: 110-117.

Chen, L.Z., Sun, W.W., Bo, L., Wang, JQ., Xiu, C., Tang, W.J., Shi, J.B., Zhou, H.P. and Liu, X.H. (2017). New arylpyrazoline-coumarins: Synthesis and anti-inflammatory activity. *Eur. J. Med. Chem.* 138:170-181.

Cho, Y.H., Kim, N.H., Khan, I., Yu, J.M., Jung, H.G., Kim, H.H., Jang, J.Y., Kim, H.J., Kim, D.I., Kwak, J.H., Kang, S.C. and An, B.J. (2016). Anti-inflammatory potential of Quercetin-3-O-β-D-("2"-galloyl)-glucopyranoside and Quercetin isolated from Diospyros kaki calyx via suppression of MAP signaling molecules in LPS-induced RAW 264.7 macrophages. *J. Food. Sci.* 81: 2447-2456.

Choi, S.B., Bae, G.S., Jo, I.J., Wang, S., Song, H.J. and Park, S.J. (2016). Berberine inhibits inflammatory mediators and attenuates acute pancreatitis through deactivation of JNK signaling pathways. Mol. Immunol. 74: 27-38.

Garrington, T.P. and Johnson, G.L. (1999). Organization and regulation of mitogen activated protein kinase signaling pathways. *Curr. Opin. Cell. Biol.* 11: 211-218.

Goldsby, R.A., Kindt, T.J., Osborne, B.A. and Kuby, J. (2003). Leukocyte Migration and Inflammation, Immunology. 5th Ed. WH Freeman and Company. New York, pp 338-360.

Handa, S.S., Chawla, A.S. and Sharma, A.K. (1992). Plants with anti-inflammatory activity. Fitoterapia. LXIII: 3-31.

Hisanaga, A., Mukai, R., Sakao, K., Terao, J. and Hou, D.X. (2016). Anti-inflammatory effects and molecular mechanisms of 8-prenyl quercetin. *Mol. Nutr. Food Res.* 60: 1020-1032.

Huang, F.C., Kuo, H.C., Huang, Y.H., Yu, H.R., Li, S.C. and Kuo, H.C. (2017). Anti-inflammatory effect of resveratrol in human coronary arterial endothelial cells via induction of autophagy: implication for the treatment of Kawasaki disease. *BMC. Pharmacol. Toxicol.* 18: 3.

Hwang, Y.J., Lee, S.J., Park, J.Y., Chun, W., Nam, S.J., Park, J.M., Park, S.C., Choi, D.H. and Kang, C.D. (2016). Apocynin suppresses lipopolysaccharide-induced inflammatory responses through the inhibition of MAP kinase signaling pathway in RAW264.7 cells. *Drug Dev. Res.* 77: 271-277.

Kang, X., Yang, Z., Sheng, J., Liu, J.B., Xie, Q.Y., Zheng, W. and Chen, K. (2017). Oleanolic acid prevents cartilage degeneration in diabetic mice via PPARγ associated mitochondrial stabilization. *Biochem. Biophys. Res. Commun.* 490: 834-840.

Lang, S., Popp, T., Kriegs, C.S., Schmidt, A., Balszuweit, F., Menacher, G., Kehe, K., Thiermann, H., Gudermann, T. and Steinritz, D. (2018). Anti-apoptotic and moderate anti-inflammatory effects of berberine in sulfur mustard exposed keratinocytes. *Toxicol. Lett.* 293: 2-8.

Li, D., Zhang, Y., Liu, K., Zhao, Y., Xu, B., Xu, L., Tan, L., Tian, Y., Li, C., Zhang, W., Cao, H., Zhan, Y.Y. and Hu, T. (2017). Berberine inhibits colitis-associated tumorigenesis via suppressing inflammatory responses and the consequent EGFR signaling-involved tumor cell growth. *Lab. Invest.* 97: 1343-1353.

Lian, J.J., Cheng, B.F., Gao, Y.X., Zhang, Y.P., Ma, S.P., Zhang, B.B., Guo, D.D., Xue, H. and Feng, Z.W. (2016). Inhibitory effect of oleanolic acid on inflammatory response in IL-1β-stimulated human synovial sarcoma SW982 cell. *Yao. Xue. Xue. Bao.* 51: 1711-1716.

Liu, C.W., Sung, H.C., Lin, S.R., Wu, C.W., Lee, C.W., Lee, I.T., Yang, Y.F., Yu, I.S., Lin, S.W., Chiang, M.H. and Liang, C.J. (2017). Resveratrol attenuates ICAM-1 expression and monocyte adhesiveness to TNF-α-treated endothelial cells: evidence for an anti-inflammatory cascade mediated by the miR-221/222/AMPK/p38/NF-κB pathway. *Sci. Rep.* 7: 44689.

Liu, H., Yang, L., Wu, H.J., Chen, K.H., Lin, F., Li, G., Sun, H.Y., Xiao, G.S., Wang, Y. and Li, G.R. (2016). Water-soluble acacetin prodrug confers significant cardioprotection against ischemia/reperfusion injury. *Sci. Rep.* 6: 36435.

Long, C., Yang, J., Yang, H., Li, X. and Wang, G. (2016). Attenuation of renal ischemia/reperfusion injury by oleanolic acid preconditioning via its antioxidant, anti-inflammatory, and anti-apoptotic activities. *Mol. Med. Rep.* 13: 4697-4704.

Ma, C., Wang, Y., Dong, L., Li, M. and Cai, W. (2015). Anti-inflammatory effect of resveratrol through the suppression of NF-κB and JAK/STAT signaling pathways. *Acta. Biochim. Biophys. Sin. (Shanghai)*. 47: 207-213.

Ma, Y. and Pope, R.M. (2005). The role of macrophages in rheumatoid arthritis. *Curr. Pharm. Des.* 11: 569-580.

Mckellar, G., Madhok, R. and Singh, G. (2007). The problem with NSAIDs: What data to believe? *Curr. Pain Headache Rep.* 11: 423-427.

Nunes, C., Almeida, L., Barbosa, R.M. and Laranjinha, J. (2017). Luteolin suppresses the JAK/STAT pathway in a cellular model of intestinal inflammation. *Food Funct.* 8: 387-396.

Payan, D.G. and Katzung, B.G. (1995). Non-steroidal anti-inflammatory drugs; Nonopoid Analgesics; Drugs used in Gout. Basic and Clinical Pharmacology, 6th Ed, Prentice Hall International, London, pp536-559.

Qin, Y.Y., Li, M., Feng, X., Wang, J., Cao, L., Shen, X.K., Chen, J., Sun, M., Sheng, R., Han, F. and Qin, Z.H. (2017). Combined NADPH and the NOX inhibitor apocynin provides greater anti-inflammatory and neuroprotective effects in a mouse model of stroke. *Free Radic. Biol. Med.* 104: 333-345.

Roitt, I., Brostoff, J. and Male D. (2001). Cell migration and Inflammation, Ed. Mosby, Immunology. 6th Ed. Gower Medical Publications, New York, pp 47- 64.

Ruland, J. and Mak, T.W., (2003). Transducing signals from antigen receptors to nuclear factor kappa B. *Immunol. Rev.* 193: 93-100.

Sandhiutami, N.M., Moordiani, M., Laksmitawati, D.R., Fauziah, N., Maesaroh, M. and Widowati, W. (2017). *In vitro* assesment of anti-inflammatory activities of coumarin and Indonesian cassia extract in RAW264.7 murine macrophage cell line. *Iran. J. Basic Med. Sci.* 20: 99-106.

Sies, H. (1993). Strategies of antioxidant defense. *Eur. J. Biochem.* 215: 213-219.

Sun, L.C., Zhang, H.B., Gu, C.D., Guo, S.D., Li, G., Lian, R., Yao, Y. and Zhang, G.Q. (2018). Protective effect of acacetin on sepsis-induced acute lung injury via its anti-inflammatory and antioxidative activity. *Arch. Pharm. Res.* 41: 1199-1210.

Sung, J. and Lee, J. (2015). Anti-inflammatory activity of Butein and Luteolin through suppression of NFκB activation and induction of Heme Oxygenase-1. *J. Med. Food.* 18: 557-564.

Wang, M., Zhao, J., Zhao, Y., Huang, R.Y., Li, G., Zeng, X. and Li, X. (2016). A new coumarin isolated from *Sarcandra glabra* as potential anti-inflammatory agent. *Nat. Prod. Res.* 30: 1796-1801.

Wang, M.T., Honn, K.V. and Nie, D. (2007). Cycloxygenases, prostanoids and tumor progression. *Cancer Metastasis Rev.* 26: 525-534.

Wu, D., Wang, Y., Zhang, H., Du, M. and Li T. (2018). Acacetin attenuates mice endotoxin-induced acute lung injury via augmentation of heme oxygenase-1 activity. *Inflammopharmacology.* 26: 635-643.

Xiong, J., Wang, K., Yuan, C., Xing, R., Ni, J., Hu, G., Chen, F. and Wang, X. (2017). Luteolin protects mice from severe acute pancreatitis by exerting HO-1-mediated anti-inflammatory and antioxidant effects. *Int. J. Mol. Med.* 39: 113-125.

Corresponding author: Dr. Debjani Sarkar, Department of Zoology, A.P.C. Roy Govt. College, Himanchal Vihar, Matigara, Siliguri, Darjeeling -734010, West Bengal, India
Email: debjani_sarkar2002@yahoo.co.in
Mobile: (+91) 7044706877