Rutuja Thopate, Shivajirao Pawar College of Pharmacy Pachegaon, Tal-Newasa, Ahmednagar, Maharashtra, India; E-mail: rutujathopate6419@gmail.com

19-Jan-2022, Manuscript No. CPB-22-51900; 21-Jan-2022, PreQC No. CPB-22-51900(PQ); 25-Jan-2022, QC No. CPB-22-51900; 29-Jan-2022, Manuscript No. CPB-22-51900(R);

of hypothalamic-pituitary-adrenal axis suppression and increased susceptibility to infections.

Mechanism of action

e short term e ects of corticosteroid are decrease vasodilation and permeability of capillaries as well as decrease leukocyte migration to site of in ammation. Corticosteroid binding to glucocorticoid receptor mediates changes in general expression that lead to multiple downstream e ect over hours to days. Glucocorticoid inhibits neutrophils apoptosis and demigrination; they inhibit phospholipase A2 which decrease the formation of arachidonic acid derivatives they inhibit NF Kappa B and other in ammatory transcription factors, they promote anti-in ammatory genes like interleukin. Lower dose of corticosteroids provide an anti-in ammatory e ect while higher dose are immunosuppressive. High dose of glucocorticoid for an extent period bind to the mineralo corticoid receptor raising sodium levels and decreasing potassium levels.

Brand name

Baycadron, Ciprodex, Decadron, Dexamethasone Intensol, Dextenza, Dioptrol, Hexadrol, Hidex 6-day Taper, Maxidex, Maxitrol, Neofordex, Ozurdex, Taperdex 12 Day Taper, Taperdex 6 Day Taper, Taperdex 7-day Taper, Tobradex, Zcort 7 Day Taper.

Uses

Dexamethasone is used to treat many di erent conditions such as allergic disorders, skin conditions, ulcerative colitis, arthritis, lupus, psoriasis, breathing disorders, eye conditions, blood cell disorders, leukemia, multiple sclerosis, in ammation.

In Vivo Screening Methods of Dexamethasone For Anti-In ammatory Agents

In this screening methods, the potency of anti-in ammatory agents are measured, by inducing the in ammation in the experimental animal like rats, mice, monkeys, dog or either sex can be selected. Before starting any in vivo assays, it is important to study the oral acute toxicity study, for the selection of test dose in this maximum tolerated dose and minimum toxic dose are calculated, by injecting the test dose at an interval of 2 hrs in 10.50.100, 200, 300.... 2000mg/kg pattern.

Acute phase: e methods that include acute phase are as follows

- Carrageenan induced paw edema in rats
- Croton-oil induced ear edema
- Oxazolone induced ear edema
- UV erythema in guinea pigs
- Pleurisy in rats
- Granuloma air pouch technique
- Vascular permeability

Chronic phase: e methods that include this chronic phase are

- Cotton wool granuloma
- Glass rod granuloma
- Sponge implantation technique

Carrageenan induced paw odema in rats

Methodology:

UV erythema in guniea pigs

Methodology: Albino guinea pigs of both the sexes weighing about 350g are used. Four animals are used each for treatment and the control, 18 hrs prior to the experiment; the animals are shaved on both the anks and on the back, chemically by means of a depilatory cream or using a suspension of barium chloride. e next day the test compound is dissolved in the vehicle and half of it is administered to the animal by gavage, 30min before the UV exposure. Control animals are treated with the vehicle alone. e guinea pigs are placed in a leather cu with a hole of 1.5x2.5cm size punched in it, allowing the UV radiation to reach only this area. During this time, the remaining half of the test compound is administered. Generally the erythema is scored a er 2 and 4 hr of exposure.

Evalution: e degree of erythema is evaluated in a double blinded

standard size and weight(10.0 ± 0.02 mg) using a 13 mm cork borer. The sponges are then soaked in 76%v/v ethanol for 30 min, and then heated at 80 for 2 hr. Prior to implantation in the animal, the sponges are soaked in sterile 0.9% saline in which drugs, antigens (or) irritants have been suspended. Sponges are implanted in female wistar rats weighing about 150-200g under ether anaesthesia.

A 20 mm dorsal incision is made and the dermis is separated from the underlying muscle layer by insertion of blunt forcepsto form separate cavities in to which the sponges are inserted [11].

Up to 8 sponges may be implanted per rat the insertion is closed with micheal clips and the animals are maintainted at a constant temperature of 24.

Evaluation: For estimation of fluid phase of sponge exudates eg: protein content enzyme levels and biological mediators such as prostaglandins as well as for leucocyte migration, sponges removed after 9 hrs.

In Vitro Screening Methods of Dexamethasone For Anti-Inflammatory Agents

- Mast cell degranulation
- Adhesion assay
- Lipopolysaccharide induced response assay
- Cyclooxygenase assay

Mast cell degranulation

During the inflammation and allergy, the mast cells are degranulated. The degree of this degranulation is a significant criterion in the pharmacological screening process of therapeutic agents against inflammation. The mast cell degranulation models are widely utilized for this study. In addition to degranulation, histamine and beta-hexosaminidase are also released, which stimulate the metabolic process of arachidonic acid. The measurement of such substances is also helpful in the pharmacological screening process for new anti-inflammatory agents. There are several methods employed to detect degranulation of mast cells and release of mediators. They include enzyme-linked immunosorbent assays (ELISAs) or colorimetric assays [12]. Colorimetric assay to measure the inflammatory mediators is rapid and sensitive. Another reported method is based on the particle analysis of granules in RBL-2H3 cells. Fluorometric assay of histamine and flow cytometric Annexin-V binding assay are also available for this purpose. The percentage release of inflammatory mediator is the index of anti-inflammatory activity.

Adhesion assay

Adhesion of leukocytes is an important cellular stage during

use. Cells were thawed in a 37°C water bath and cultured overnight in RPMI1640 medium containing 10% feta lbovine serum, 1% penicillin-streptomycin-glutamine,1% MEM non-essential amino acids solution, 15 mm HEPES, 1 mm sodium pyruvate and 55 µM2-mercaptoethanol. Cells were plated at 1*105/200 µlin 96-well round-bottom plates with M-450 Tosylactivated beads. Dexamethasone was purchased from Sigma Aldrich (D4902) and dissolved in DMSO. Niviolumab and ipilimumab F(ab')2 were used to block PD-1 and CTLA-4, respectively. Ipilimumab F(ab')2 was created using a Pierce F(ab')2 Preparation Kit per the manufacturer's instructions (ermo Fisher Scienti c, MA, USA). Cells were incubated at 37 °C in 20% O2, and 5% CO2 for four days for proliferation analyses and two days for Western blot and qPCR analyses.

Western blot analysis

Isolated human T cells were collected a er 48 h of stimulation and lysed in RIPA bu er with EDTA- free protease inhibitor cocktail set III (EMD Millipore, Billerica, Massachusetts, USA). Pierce BCA protein assay kit (ermo Fisher Scienti c, Rockford, IL, USA) was used to determine protein concentration. Sample swere separated by SDS-PAGE (Bio-Rad) and transferred onto 0.2 µm pore size poly vinylidene uoridemembranes (PVDF) (In vitrogen, Carlsbad, CA, USA). e following antibodies were purchased from Cell Signaling: cleaved caspase 3 (5A1E), p27kip (2552 s),cyclin D3 (DCS22), CDK4 (D9G3E). Anti-CTLA-4(EPR1476) was purchased from Abcam. e bandswere detected by Super Signal West Pico chemiluminescence reagent (Pierce, Rockford, IL, USA). Anti-bodiesagainst -actin (AG74) or GAPDHstandard were used as internal standards.

Conclusion

Anti-in ammatory agent the several in vitro methods are developed for the pharmacological screening of anti-in ammatory activity. Many of the method re ect In vivo performance. ese methods help to understand the real mechanism of in ammation and to identify new compounds possessing the anti-in ammatory activity. It is very di cult to develop single in vitro method for anti-in ammatory activity. Even in future. e mentioned method will accelerate the anti-in ammatory drug development process. e impact of dexamethasone on T cell subsets in the setting of immunotherapy. Dexamethasone blocks naïve T cell proliferation and di erentiation by attenuating CD28 co-stimulation. Because co-stimulation is essential for successful T cell priming and expansion, these data suggest that corticosteroid similar response in immunotherapy treatment-naïve patients or those with poorly antigenic tumors. However, T cells may be partially protected

with administration5if CTLA-4 blockade. Additionally, negative

tumor immune response.

1. Koh TJ, DiPietro LA (2011) Q}'æ{ {æcā[}Áæ}åÁ¸[˘}åÁ@^æ|ā}*ÁV@^Á¦[|^Á[-Ác@^Á macrophage. Expert Rev Mol Med 13:e.
2. Nourshargh S, Alon R (2014) Š^˘\[&^c^Á {ā*¦æcā[}Áā}c[Áā}'æ{^åÁcā••˘^•Ė Immunity 41:694-707.
3. Hughes JP, Rees S, Kalindjian SB, Philpott KL (2011) Principles if early drug discovery. Br J Pharmacol 162:19-1249.
4. Joo T, Sowndhararajan K, Hong S, Lee J, Park SY, et al. (2014) Inhibition if nitric oxide production In LPS-stimulated RAW 264.7 cells by stem bark if Ulmus pumila L. Saudi J Biol Sci 21:427-435.
5. Langer HF, Chavakis T (2009) Leukocyte-endothelial interactions in ā}'æ{ {æcā[}Ė J Cell Mol Med 13:1211-1220.
6. Wildner O, Lipkow T, Knop J (1992) Increased expT1 Inon if ICAM-1 E-selectin, and VCAM-1 by Cultured human endothelial cells upon expoTJre to haptens. Exp Dermatol 1:191-198.
7. Schön MP, Krahn T, Schön M, Rodriguez ML, Antonicek H, et al. (2002) Ò-[{ˆ&ā}^ÁTĖÁæÁ}^¸ÁÙ]^&ā,&Áā}@āàāc[¦Á[-Á•^|^&cā}ĖÁā{]æā¦•Á|^˘\[&ˆc^Áæå@^•ā[}Áæ}åÁæ||^çāæc^•Á&˘cæ}^[˘•Áā}'æ{ {æcā[}Ė Nat Med 8:366-372.
8. Pè\æ}•[}ÁÜĖÁÜ4}}à^¦*ÁŒŠÁÇFJĬIDÁQ{]¦[ç^åÁ'˘[¦[{^c¦ā&Áæ••æˆÁ[-Á@ā•cæ{ā}^ÁÁ Condensation5with Ophthalaldehyde at -20. Anal Biochem 60:560-567.
9. Taylor ML, Ilton MK, Misso NL, Watkins DN, Hung J, et al. (1998) V@^Á^ ^&cÁ[-Á aspirin on Thrombin stimulated platelet adhesion5receptor expT1 Inon and the role if neutrophils. Br J Clin Pharmacol 46:139-145.
10. Lee MH, Lee JM, Jun SH, Ha CG, Lee SH, et al. (2007) In-*vitro* and n-*vivo* anti-ā}'æ{ {æc[¦ˆÁŒ&cā[}Á[-Ác@^Á^c@æ}[|Á^¢c¦æ&cÁ[-Ác¦æ&@^|[•]^¦{ā&æ˘|ā•Ė J Pharm Pharmacol 59:1-130.
11. Reis J, Guan XQ, Kisselev AF, Papasian CJ, QJreshi AA, et al. (2011) LPS-ā}å˘&^åÁØ[¦{æcā[}Á[-Áā{{˘}[]¦[c^æ•[{^•ÁVÞØĖ Áæ}åÁ}āc¦ā&Á[¢āå^Á]¦[å˘&cā[}Á are regulated by altered CompoTition if proteasome-active Tites. Cell BiochemBiophys 60:77-88.
12. Chen Y, Junger WG (2012) MeasJrement if oxidative burst in neutrophils. Methods Mol Biol 844:115-124.
13. Chow LW, Yip AY, Chu WP, Loo WT, Toi M. (2011) Bone metabolism and quality-of-life if Postmenopausal women with invasive breast cancer receiving neoadjuvant hormonal therapy: Sub-analyses from celecoxib anti-aromatase neoadjuvant (CAAN) trial. J Steroid Biochem Mol Biol 125:112-119.
14. Sung-Hwan E, Eun-Hye L, Kunbawui P, Ji-Young K, Poong-Ho K, et al. (2016) Ò&\[|Á-¦[{ÁÒā•^}āæÁàā&ˆ&|ā•Áā}@āàāc•Áā}'æ{ {æcā[}Ác@¦[˘*@Ác@^ÁŒ\cÐÞØĖ àÁ signaling in propionibacterium acnes-Induced human keratinocyte hacat cells. J Food Biochem 41:e112.
15. T[@æ{{^åÁÞŒĖÁŒàåÁÒ|ĖŒ|^^{ÁÙŒĖÁÒ|ĖPæ,:ÁPŒĖÁT&Tæ@[}ÁÜØÁÇG€€IDÁ Distribution if constitutive (COX-1) and inducible (COX-2) cyclooxygenase In poTtviral human liver cirrhoTis: A poTsible role for COX-2 in the PathogeneTis if liver cirrhoTis. J Clin Pathol 57:350-354.
16. Resch M, Steigel A, Chen ZL, Bauer R (1998) 5-lipoxygenase and Cyclooxygenase-1 inhibitory active compounds from Atractylodeslancea. J Nat Prod 61:347-350.
17. Petrovic N, Murray M (2010) Using N,N,N',N'-tetramethyl-p-Phenylenediamine (TMPD) to assay cyclooxygenase activity in vitro. In: Armstrong D, editors. Advanced Protocols in Oxidative Stress II. Methods in Molecular Biology (Methods and Protocols). Totowa, New Jersey: Humana Press 594.
18. Copeland RA, Williams JM, Giannaras J, Nurnberg S, Covington M, et al. (1994) Mechanism if selective inhibition if the inducible isoform if Prostaglandin G/H synthase. Proc Natl Acad Sci USA 91:11202-11206.
19. Farber SH, Tsvankin V, Narloch JL, Kim GJ, Salama AK, et al. (2016) Embracing rejection: Immunologic trends in brain metastaTis. Oncoimmunology 5:1172153.
20. Fecci PE, Ochiai H, Mitchell DA, GroTsi PM, Sweeney AE, et al. (2007) Systemic CTe14 Blockade ameliorates glioma-induced changes to the CD4+T &^||Á&[{]æ¦c{^}cÁ¸āc@[˘cÁæ ^&cā}*ÁÜ^*˘|æc[¦ˆÁVĖ&^||Á-˘}&cā[}Ė Clin Cancer Res 13:2158-2167.
21. Larkin J, Hodi FS, Wolchok JD (2015) Combined Nivolumab and Ipilimumab or monotherapy in Untreated melanoma. N Engl J Med 373:1270-1271.
22. Weber JS, Kahler KC, Hauschild A (2012) Management if immune-related adverse events and Kinetics if response with ipilimumab. J Clin Oncol 30:2691-2697.
23. Jijith US, Jayakumari S (2018) In *vitro* pharmacological screening Methods for æ}cāĖā}'æ{ {æc[¦ˆÁæ*^}c•Ė Asian J Pharma Clin Res 11.