

oxygenase inhibitor 가 MTS가 formazan , 490nm 가 3 Prizm t-test

대상 및 방법

P100 plate . low pa - ssage , trypsin - EDTA resuspend , 96 well plate 1 well 8000 10% FBS(Fetal Bovine Serum) - MEM(Minimum Essential Medium) 24 . 0.5% FBS - MEM 48 starvation , well inhibitor , 가 가 . Inhibitor , cyclooxygenase inhibitor indomethacin(25, 100, 150 μ M), lipoxygenase inhibitor NDGA(5, 10, 20 μ M) 5 - lipoxygenase AA861(5, 10, 20, 40 μ M), AKBA (5, 10, 20, 30 μ M) . inhibitor 가 96 , methyl tetra - zolium salt/phenazine methosulfate(MTS/PMS) assay (CellTiter 96 Aqueous nonreactive cell proliferative assay, Promega) . MTS/PMS assay well MTS/PMS 20 μ 6 ELISA plate reader 490nm wavelength UV optical density 가 dehydrogenase enzyme

결 과

5 - lipoxygenase inhibitor AA861

(Fig.

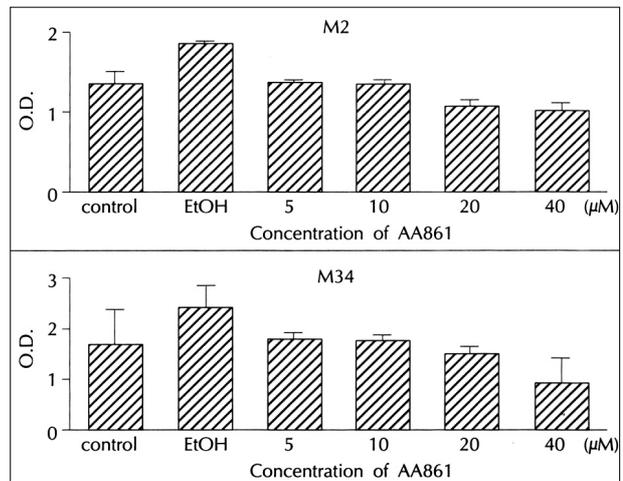


Fig. 2. Effect of AA861 (5-LO inhibitor) on the proliferative of meningeoma cells. There was no inhibition of proliferation. O.D : optical density M2, M34 : cultured meningeoma cell lines EtOH ; Ethanol, -used as a solvent of AA861

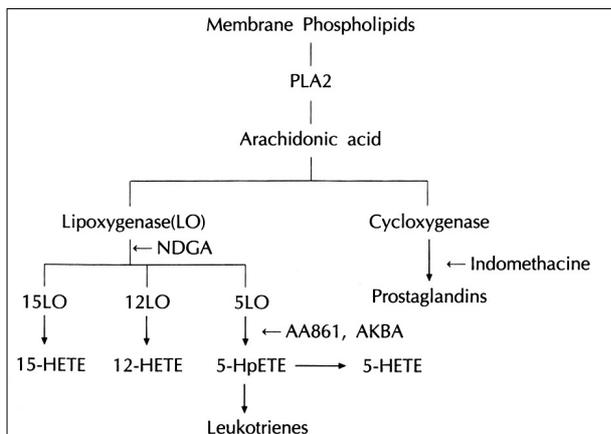


Fig. 1. Schematic representation of the various enzymes and inhibitors in major pathways of arachidonic acid metabolism. PLA₂ : cytosolic phospholipase2 NDGA : No-dihydroguaiaretic acid AKBA : aetyl-11-keto-beta-boswellic acid 5-HpETE : 5-hydroperoxyeicosatetraenoic acid 5-HETE : 5-hydroxyeicosatetraenoic acid

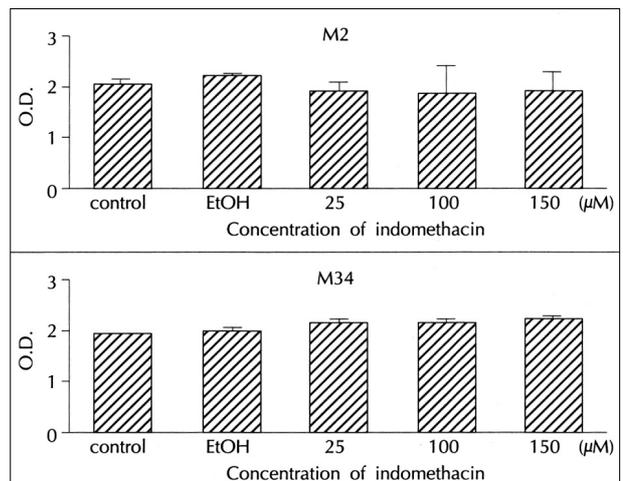


Fig. 3. Effect of indomethacin(CO inhibitor) on the proliferative of meningeoma cells. There was no inhibition of proliferation. O.D : optical density M2, M34 : cultured meningeoma cell lines EtOH : Ethanol, -used as a solvent of indomethacin

2). Cyclooxygenase inhibitor indomethacin lipo-
xygenase inhibitor NDGA

(Fig. 3, 4). AKBA

(Fig. 5).

고찰

가

9)22)24)27)29)43)46)60)

50%

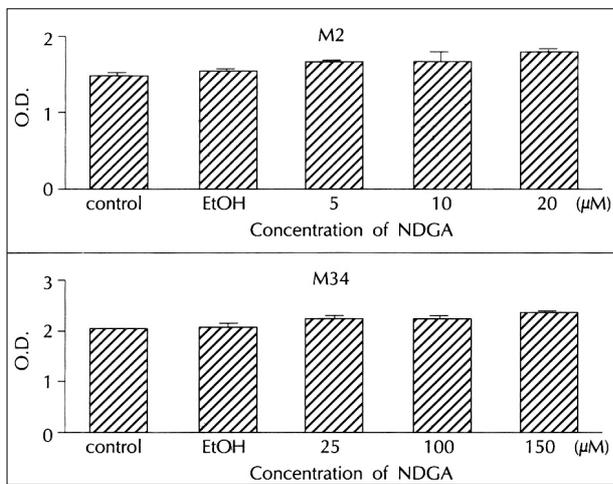


Fig. 4. Effect of NDGA(5-LO inhibitor) on the proliferative of meningioma cells. There was no inhibition of proliferation.
O.D : optical density
M2, M34 : cultured meningioma cell lines
EtOH : Ethanol, - used as a solvent of NDGA

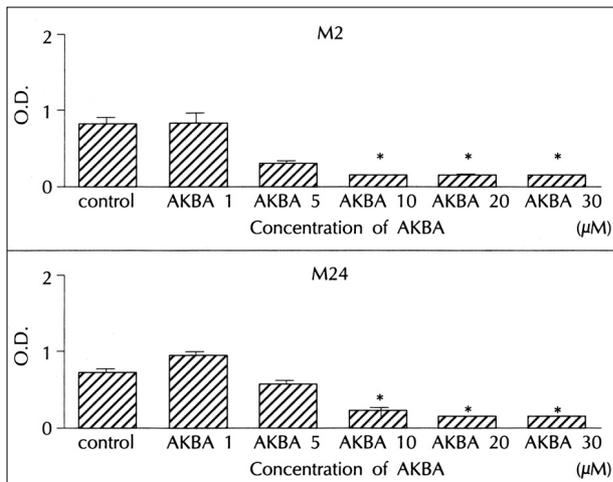


Fig. 5. Effect of AKBA(5-LO inhibitor) on the proliferative of meningioma cells. There was no inhibition of proliferation.
O.D : optical density
M2, M34

32)44)

가

(membrane phospholipid)

가

eicosanoid가, lipoxygenase cyclooxygenase pathway arachidonic acid

20)

phosphatidylinositol, sphingomyelin, lyso-phosphoglyceride 가

oleic, linoleic, arachidonic acid

가 가

34). Cooper¹⁴⁾

prostaglandin, prostacyclin, throm-

boxane

. Stein⁵⁶⁾

linoleic palmitoleic acid가 가, stearical pal-mitic acid

. Hattori²⁶⁾

Prostaglandin

38)

prostaglandin

3)15)17)30)46)58)59). Ledwozyw³⁴⁾

prostaglandin

20%가 bone resorption new bone formation

, PGE2가 bone re-sorbing agent prostaglandin

leukotriene prostaglandin

가

가 prostaglandin level 가

16)24)

prostaglandin

13)31)33)

prostaglandin

17)15)24)30)39)40)48)

lipoxy-

genase inhibitor cyclooxygenase inhibitor가

4)22).
 arachidonic acid(AA)
 6). cytosolic phospholipase A2(cPLA2)
 arachidonic acid lipoxxygenase cyclooxygenase leukotriene prostaglandin (Fig. 1).
 oncogene , virus 가
 14). On-cogene 가
 growth factor autocrine, paracrine effect
 . cPLA2 EGF(epidermal growth factor), IL - 2, IFN - , MAP kinase phosphorylation
 5)10)35)36)53). Sato⁵³⁾
 EGF PGE2 2 가
 , 10
 EGF AA release cPLA2 activity 가
 , EGF cyclooxygenase - 2(COX - 2) 가
 , COX inhibitor in vivo
 17)30)39)48), in vitro 가
 12)52). LO inhibitor in vivo in vitro 가
 가 18)42)55). 5 - LO leukotriene 가
 . leukotriene 가
 volume growth ,
 corticosteroid leukotriene
 18)42)55). cyclooxygenase
 COX - 1 COX - 2가 COX - 1
 , COX - 2가 prostaglandin
 . lipoxxygenase 3가 , 5 - LO, 12 - LO, 15 - LO가 . 5 - LO leukotriene pro - inflammatory role 가
 . leukotriene slow reacting substance of anaphylaxis(SRS - A)
 5 - LO inhibitor 가 19)20). Gati¹⁹⁾
 archidonic acid prostaglandin, leukotriene , vo -
 lume growth 3H - thymidine labelling , COX inhibitor indomethacine intermediate concentration

(0.5 5.0 µg/ml) , 50 µg/ml
 , COX LO inhibitor keto - profen (50 µg/ml)
 , LO inhibitor NDGA cell spheroid
 , quinacrine spheroid growth rate . Gati²¹⁾
 3H - thymidine uptake leukotriene 5 - lipoxxygenase inhibitor AA - 861
 , AA - 861 monolayer 가
 , heat Ca++ ionophore 가 ,
 B4 leukotriene 가
 . Arachidonic acid
 8)23)54)57). , ,
 arachidonic acid가
 , arachidonic acid 5 - LO product가
 , Ras protein negative regulator GTPase activating protein(GAP) neurofibromin(NF1)
 23), , poly - peptide growth factor receptor가 over - expression , 5 - LO metabolite가 signal transduction process 8)54)57)
 eicosanoid
 CO inhibitor indomethacin, LO inhibitor NDGA 5 - LO AA861, AKBA
 . COX inhibitor indomethacin LO inhibitor NDGA
 , 5 - LO inhibitor AA861
 , . 5 - LO inhibitor AKBA
 control . AKBA
 50% (inhibition concentration) 4 6 µM (Fig. 6).
 Leukotriene key enzyme 5 - LO가 ,
 , Crohn's disease, shock circulatory disease hyper - sensitivity based disease inhibitor target

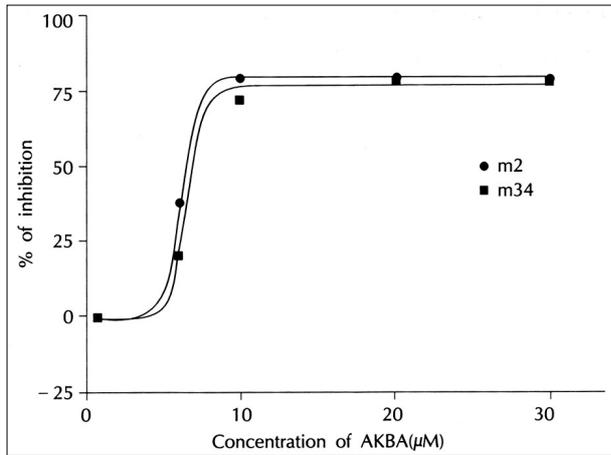


Fig. 6. Percent inhibition of meningioma cell proliferation with AKBA. The 50% inhibition concentration(IC50) of AKBA was 4 - 6 μ M. M2, M34 : cultured meningioma cell lines

60). AKBA 5-LO boswellic acid . Bos-wellic acid Boswellia serrata

49). Boswellia gum resin 82% remission 25).

5-LO inhibitor가 redox cycler radical scavenger

5-lipoxygenase inhibitor redox-type inhibitor

51). AKBA pentacyclic triterpene 5-LO , arachi-donate substrate binding site . Safayhi boswellic acid가 leukotriene

50). 5-LO human leukocyte elastase(HLE) 가 AKBA inhibit , HLE inhibitory effect pentacyclic triterpene 5-LO , leukotriene chemical agent(NDGA, MK - 886, ZM - 230,487) HLE activity

50). Heldt 28) leukotriene E4(LTE4)가 ,

LTE4 volume boswellic acid Boswellia serratia , cysteinyl-leukotriene

NDGA indomethacine

5-lipoxygenase가 cytoskeletal protein actin polymerization 45)

5-lipoxygenase inhibitor

AA861 AKBA 가 5-lipoxygenase , 5-lipoxygenase가 AKBA 가 AKBA

in vivo study AKBA in vivo study

결론

AKBA inhibitor Indomethacin, NDGA, AA861 가

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