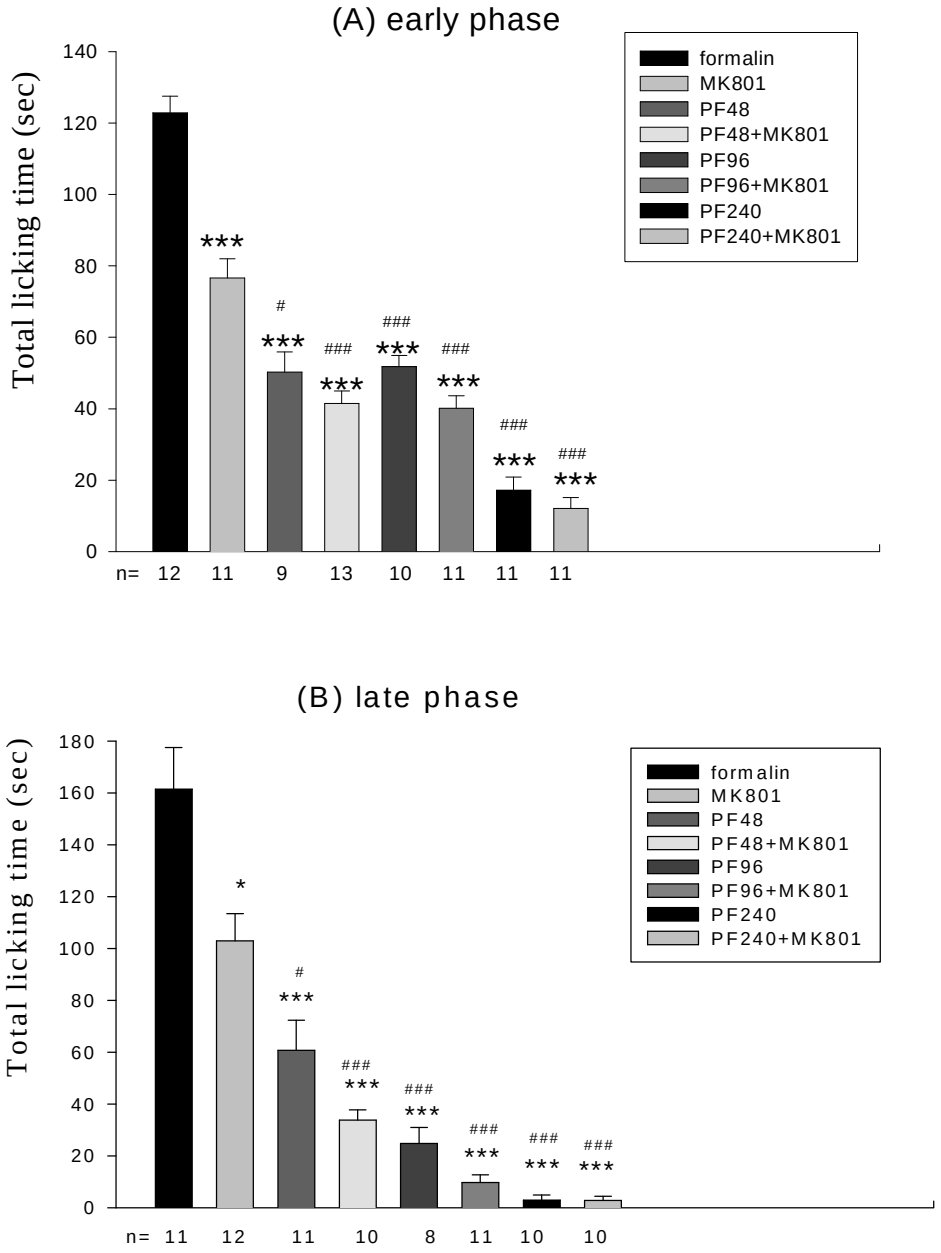

Fig 1.The effect of paeoniflorin on MK-801-treated mice in formalin test.
Paeoniflorin (PF 48, 96, 240 μg / 5μl) were intracerebroventricularly administered 15min before intraplantar injection of 20μl 1% formalin. MK-801 (MK 5 ng /5μl) was administered intrathecally 5min before formalin injected. Data were shown as mean ± S.E..
* P<0.05, ** P<0.01, *** P<0.001 compared with control group.
# P<0.05, ## P<0.01, ### P<0.001 compared with MK-801 group

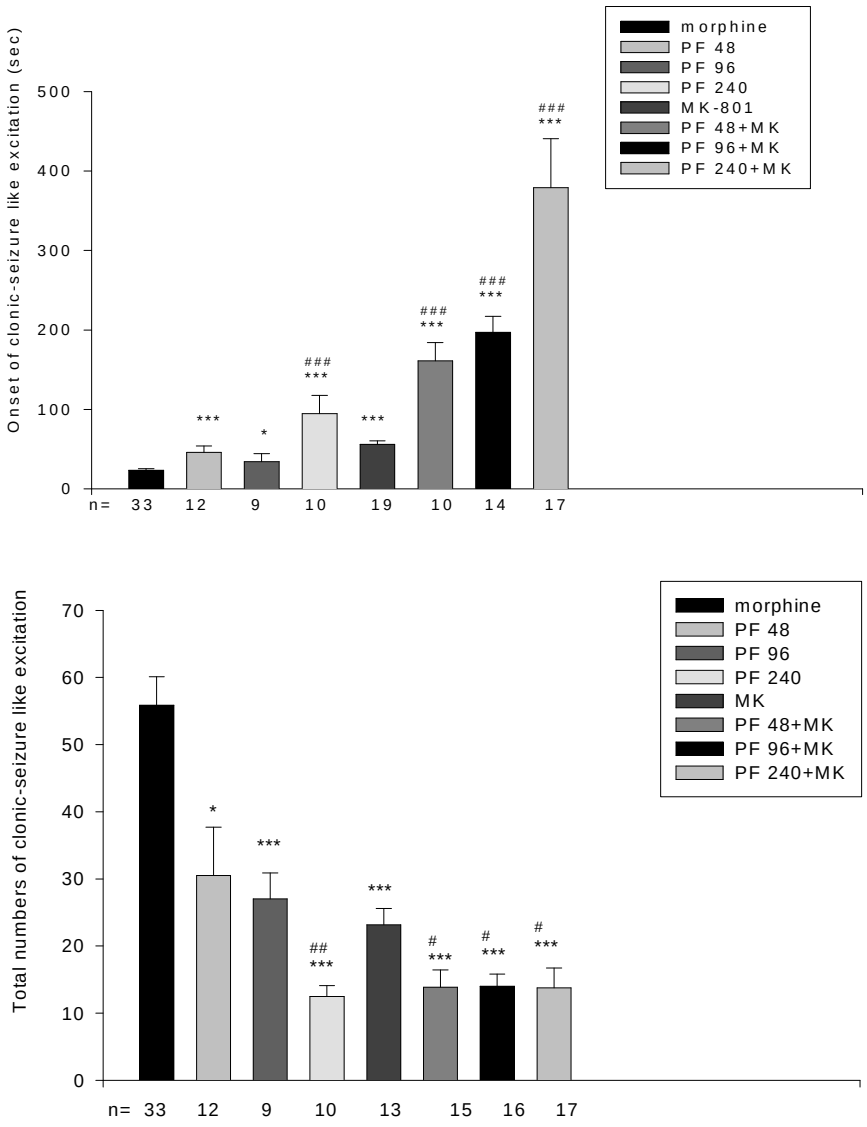

Fig 2.Effect of combination administration of paeoniflorin and NMDA receptor antagonist MK-801 on high dose morphine-induced clonic-seizure like excitation duration 1 hour. Paeoniflorin (PF 48, 96, 240 μg / 5μl) were intracerebroventricularly (i.c.v.) administered 15 min before intrathecal of morphine (80 μg / 5μl). MK-801 (MK 18 ng / 5μl) were intrathecal (i.t.) administrated 5 min before morphine. The onset time and total numbers of clonic-seizure like excitation induced by morphine during the first 60 min after morphine injected was recorded. Data were shown as mean ± S.E.
P<0.05, ** P<0.01, *** P<0.001 compared with morphine group.
# P<0.05, ## P<0.01, ### P<0.001 compared with MK-801group.

Tab 1. Effect of paeoniflorin on strychnine-induced seizure and motality in mice.

	Strychnine 5μl		Paeoniflorin 48 μg + Strychnine 5μl		Paeoniflorin 96 μg + Strychnine 5μl		Paeoniflorin 240 μg + Strychnine 5μl	
	onset	duration	onset	duration	onset	duration	onset	duration
Mean ± S.E.	16.5±2.7	232.6± 47.7	20.3± 2.2	139.2± 40.5***	19.2±1.4	217.7± 48.4	26.5± 4.5*	210.8± 59.5
Seizure / total	26/26(100%)		25/25(100%)		18/22 (81.8%)***		13/20 (65%)***	
Death / total	14/26 (53.8%)		8/25 (32%)		3/22 (13.6%)***		7/20 (35%)	

Data represented as mean ± S.E.

*P<0.05, **P<0.001, ***P<0.0001 compared with control group

Seizure / total: numbers of seizure / total numbers of mice.

Death / total: numbers of death mice / total numbers of mice

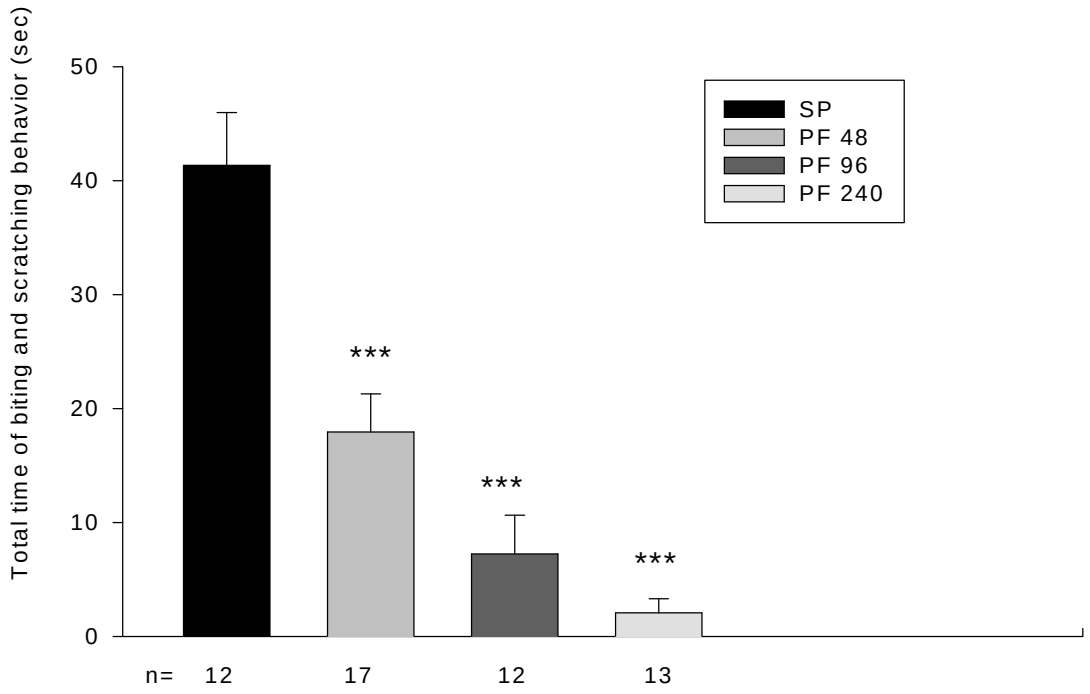

Fig 3.The effect of paeoniflorin on substance P (SP)-induced biting and scratching behavior in mice. Paeoniflorin (PF 48, 96, 240 μg/5μl) were intracerebroventricularly (i.c.v.) administered 15 min before intrathecal of SP (10 ng/5μl). The time spent biting or scratching induced by SP during the first 120s after SP injected was recorded. Data were shown as mean ± S.E.

*** P<0.001 compared with substance P group.

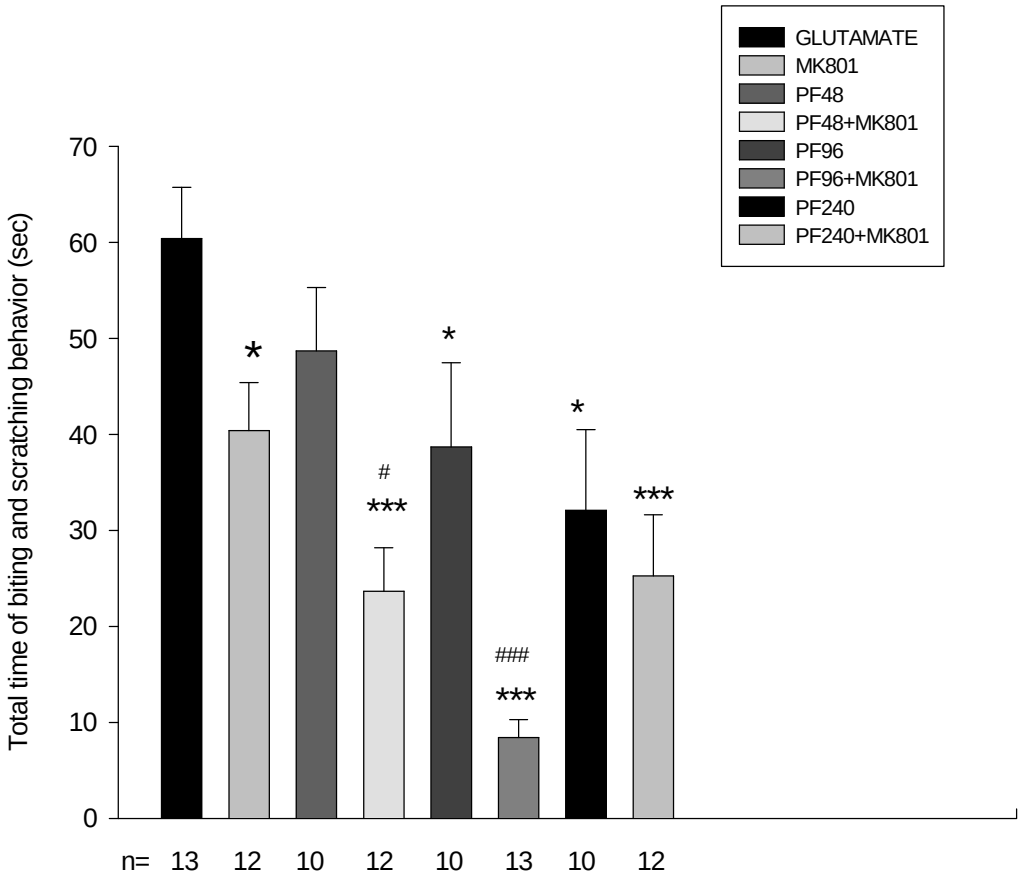

Fig4.The effect of paeoniflorin and MK 801 on glutamate-induced biting and scratching behavior in mice. Paeoniflorin (PF 48, 96, 240 μg /5μl) were intracerebroventricularly (i.c.v.) administered 15min before intrathecal injection of glutamate (500 nmol /5μl). NMDA receptor antagonist MK 801 (5 ng /5μl) was administered intrathecally 5 min before glutamate injection. The time spent on biting or scratching induced by glutamate during the first 120s after glutamate injection was recorded. Data were shown as mean ± S.E.

* P<0.05, ** P<0.01, *** P<0.001 compared with glutamate-treated group.

\# P<0.05, ## P<0.01, ### P<0.001 compared with MK-801-treated group.

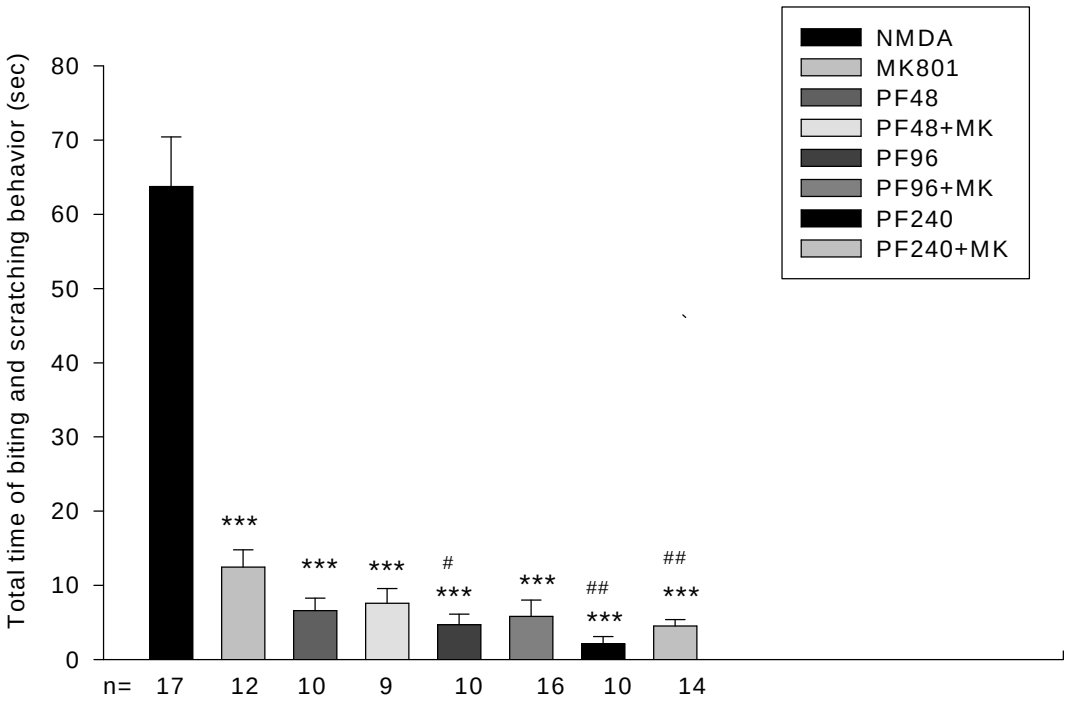

Fig 5.The effect of paeoniflorin and MK 801 on NMDA-induced biting and scratching behavior in mice. Paeoniflorin (PF 48, 96, 240 μg/5μl) were intracerebroventricularly (i.c.v.) administered 15 min before intrathecal of NMDA (122 pmol /5μl). NMDA receptor antagonist MK-801 (MK 5ng/5μl) was administered intrathecally 5 min before NMDA injected. The time spent biting or scratching induced by NMDA during the first 120s after NMDA injected was recorded. Data were shown as mean ± S.E.

* P<0.05, ** P<0.01, *** P<0.001 compared with NMDA group.

# P<0.05, ## P<0.01, ### P<0.001 compared with MK-801-treated group.

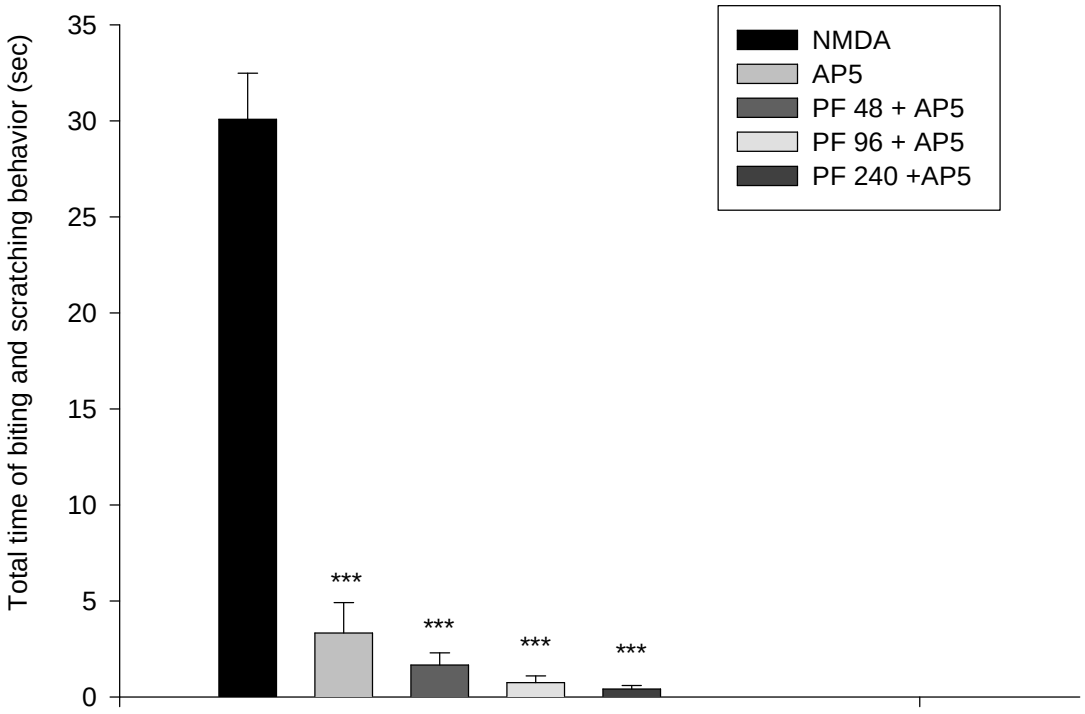

Fig 6.The effect of paeoniflorin and AP5 on NMDA-induced biting and scratching behavior in mice. Paeoniflorin (PF 48, 96, 240 μg /5μl) were intracerebroventricularly (i.c.v.) administered 15min before intrathecal injection of NMDA (122 pmol /5μl). NMDA receptor antagonist AP5 (0.1 mM /5μl) was administered intrathecally 5 min before AMPA injected. The time spent on biting or scratching induced by NMDA during the first 120s after injection NMDA was recorded. Data are shown as mean ± S.E. (n=12)

* P<0.05, ** P<0.01, *** P<0.001 compared with NMDA group.

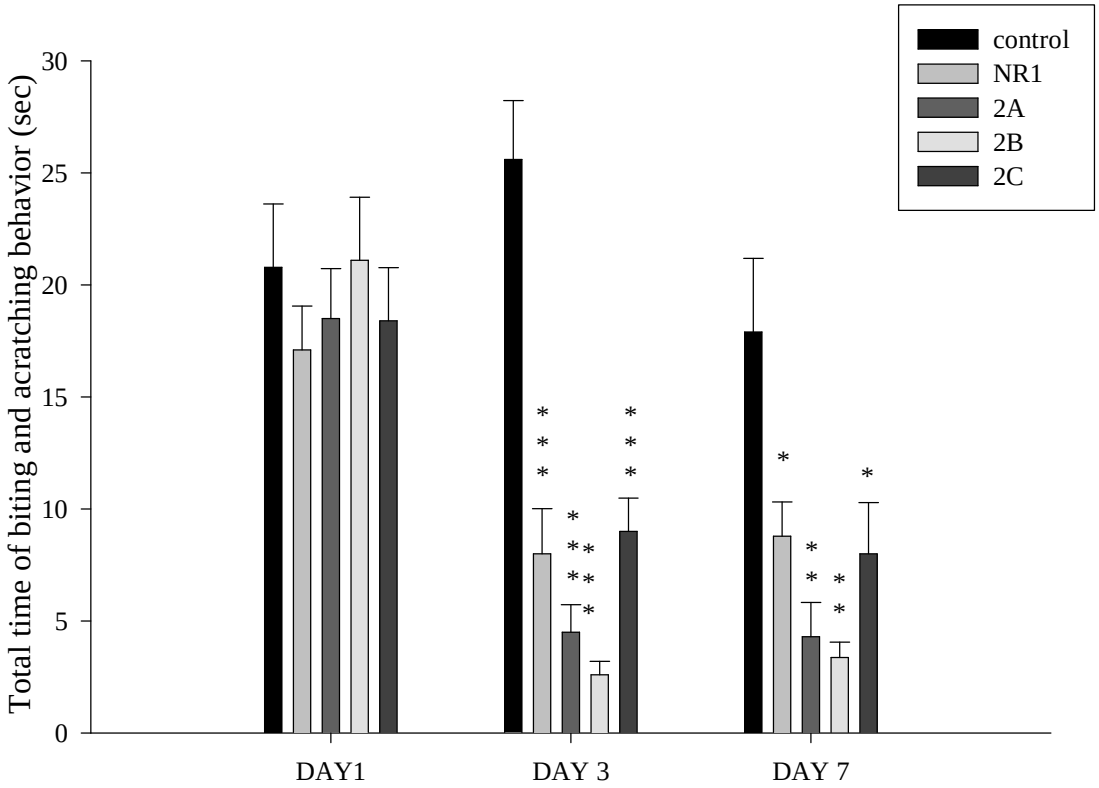

Fig 7. The time course effect of antisense oligodeoxynucleotides of NMDA receptor subunits on NMDA-induced biting and scratching behaviors in mice. Antisense oligodeoxynucleotides (15 nM / 5μl) were intracerebroventricularly administered 1, 3, 7 days before intrathecal of NMDA (122 pmol / 5μl). The time spent biting or scratching induced by NMDA during the first 120s after NMDA injected was recorded. Data are shown as mean ± S.E.
* P<0.05, ** P<0.01, ***P<0.001 compared with NMDA group.

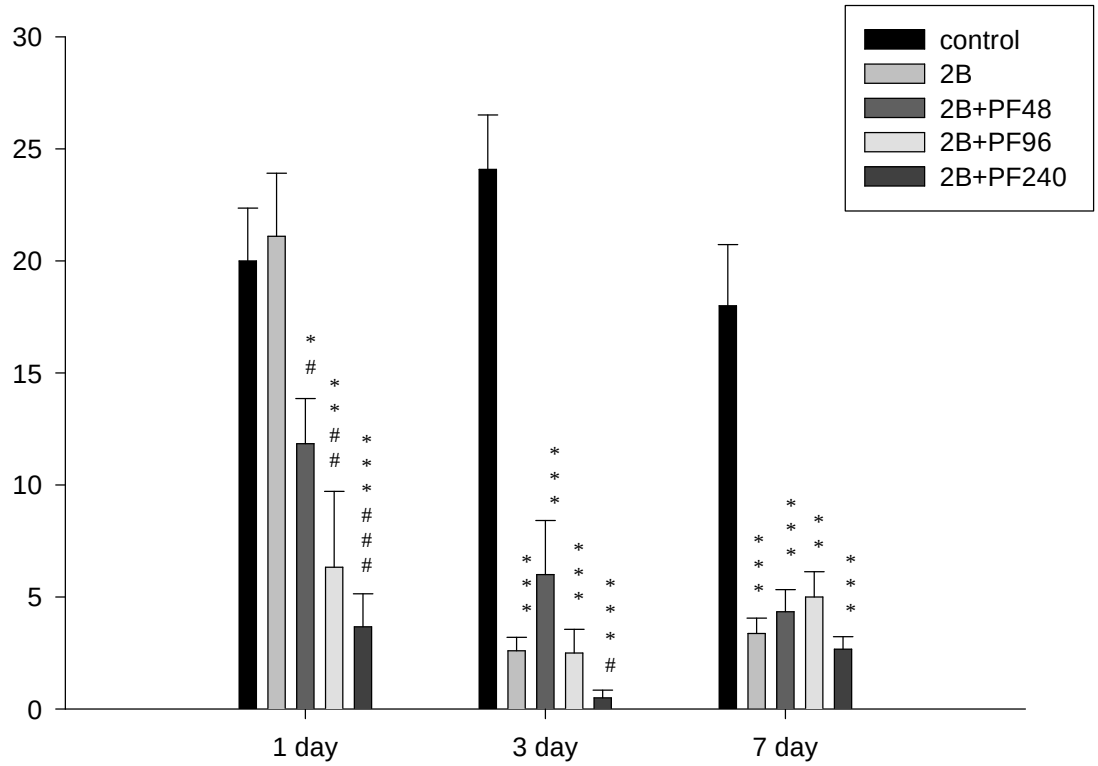

Fig 8. Effect of antisense oligodeoxynucleotide of NMDA receptor subunit (2B) on NMDA-induced biting and scratching behavior in mice. Paeoniflorin (PF 48, 96, 240 μg / 5μl) were intracerebroventricularly (i.c.v.) administered 15 min before intrathecal of NMDA. Antisense oligodeoxynucleotide (15 nM / 5μl) were intracerebroventricularly administered 1, 3, 7 days before intrathecal of NMDA (122 pmol / 5μl). The time spent on biting or scratching behavior induced by NMDA during the first 120s after NMDA injection was recorded. Data were shown as mean ± S.E.

* P<0.05, ** P<0.01, *** P<0.001 compared with NMDA group.

# P<0.05, ## P<0.01, ### P<0.001 compared with antisense 2B group.

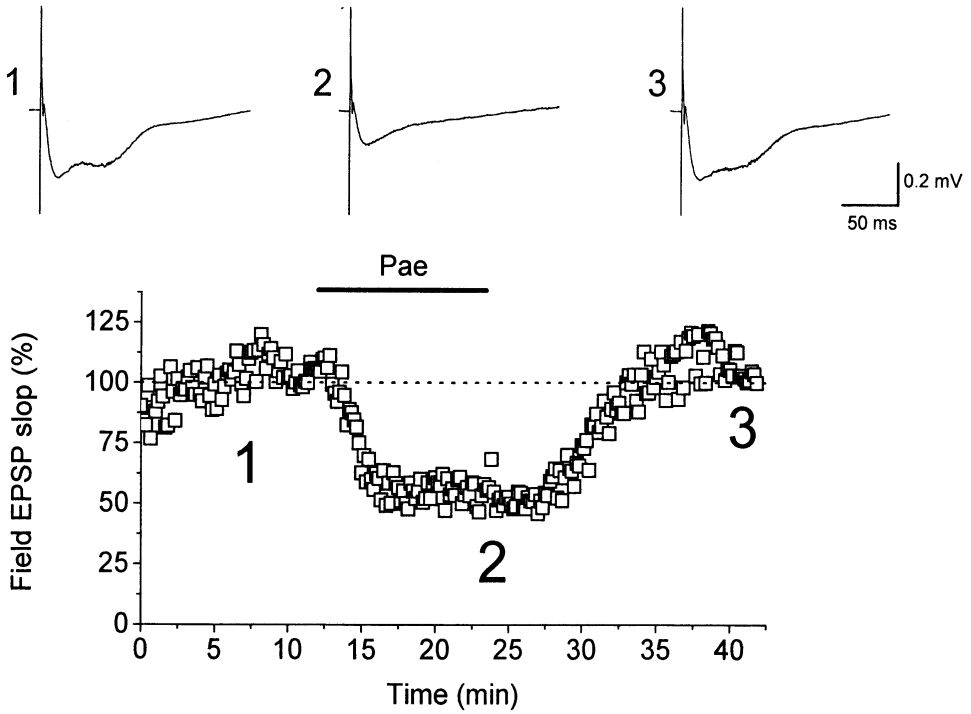

Fig 9. Effect of 2μM paeoniflorin on NMDA receptor mediated excitatory postsynaptic potential in rat hippocampal brain slice.

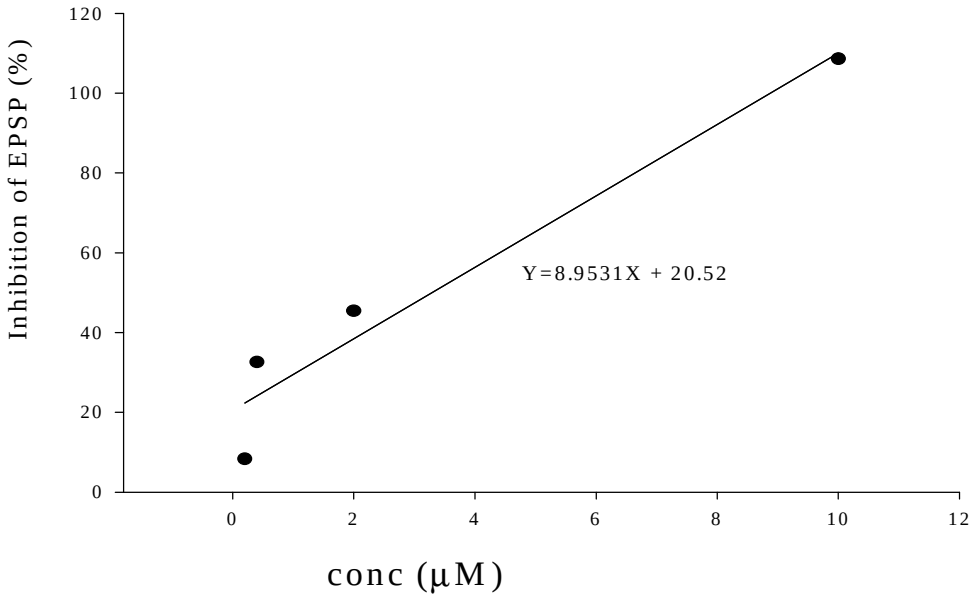

Fig 10. Effect of paeoniflorin on NMDA receptor mediated excitatory postsynaptic potential in rat hippocampal brain slice.