Figure S1. The photograph of tumors in sh-GFP and sh-Aurora B shRNA group. A, The photograph of HepG2 cells; B, the photograph of Hep3B cells.

Figure S2. Butein was identified through the compound screening. A, the structure of natural compounds used for screening. B, HepG2 cell lysates (400 mg) was incubated with compound-Sepharose 4B beads (Sepharose 4B beads only as control) overnight at 4°C, and the beads were subjected to western blotting. C, HepG2 cells were treated with 10 μM of natural compounds, cell viability was accessed by MTS assay. *, $p<0.05$.

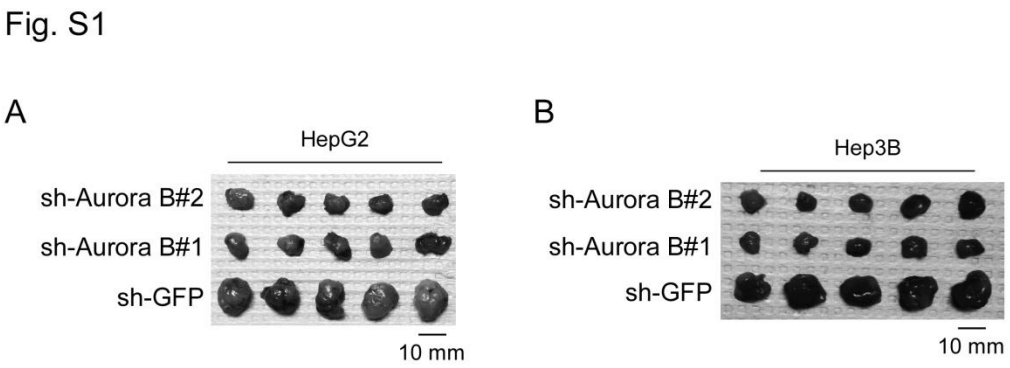
Figure S3. Butein did not bind with Aurora A or Aurora C. HepG2 (left) and Hep3B (right) cell lysates were incubated with butein-Sepharose 4B beads (Sepharose 4B beads only as control) overnight at 4°C, and the beads were subjected to western blotting for Aurora A (A) or Aurora C (B) determination.

Figure S4. Butein did not inhibit Aurora A/C kinase activity in vitro. Inactive Histone H3.3 protein was incubated with different concentrations of butein, active Aurora A/C kinase and 100μM ATP reaction buffer at 30°C for 30 min, the phosphorylation of histone H3 was examined by western blotting, Hesperadin/Danusertib was used as positive control.

Figure S5. The inhibitory effect of butein on normal LO2 cells. A, LO2 cells were treated with butein for 24 h, whole cell extracts were subjected to western blot analysis as indicated. #, not statistically significant. B, LO2 cells were treated with butein for 24 h and subjected to cell cycle analysis by flow cytometry. left; the representative FACS results, right; statistical analysis of three independent experiments.

Figure S6. Butein inhibited HepG2 and Hep3B xenograft growth *in vivo*. A-B, the photographs of tumors of HepG2 (A) and Hep3B (B) xenograft experiments. C-D, the body weight of nude mice bearing HepG2 (C) and Hep3B (D) xenograft during the efficacy studies.

Supplementary Figure 1



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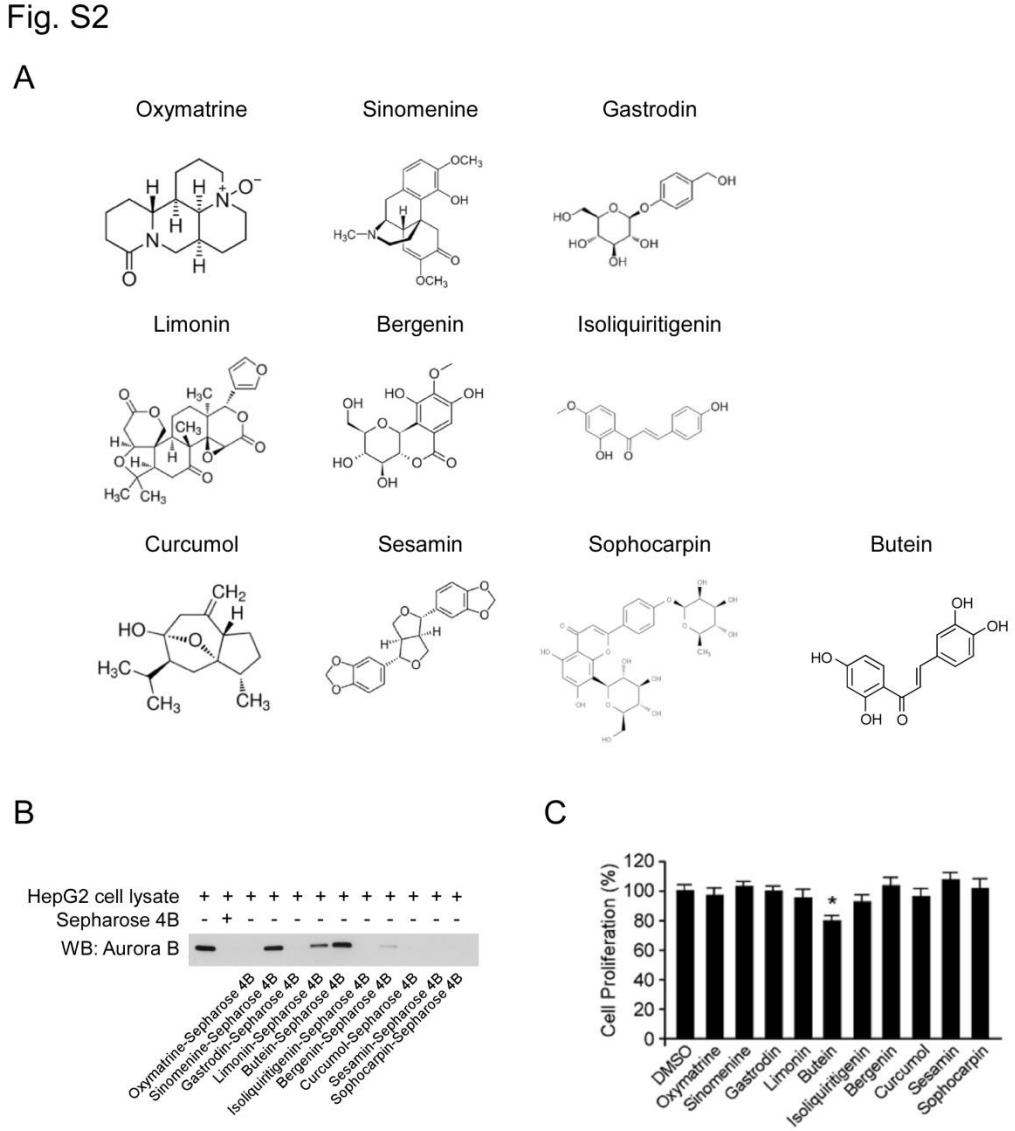
Supplementary Figure 2



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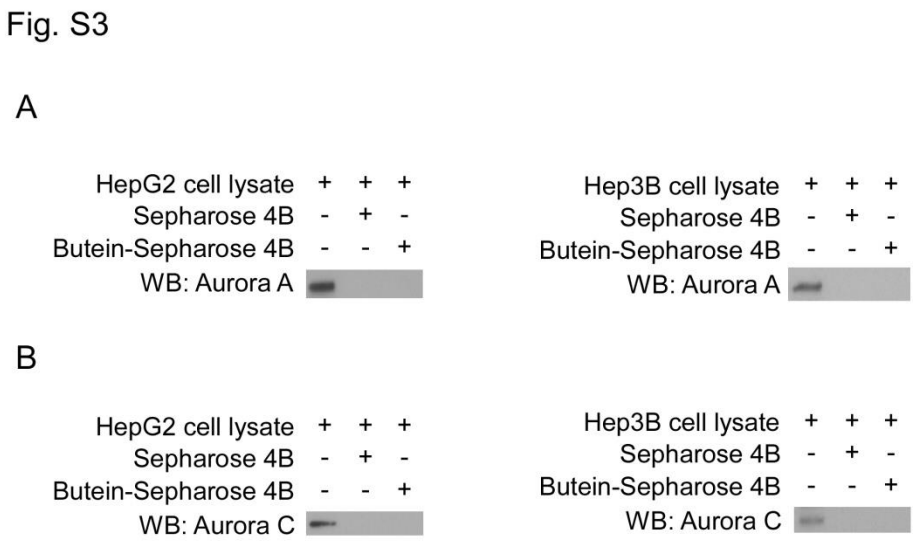
Supplementary Figure 3



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Supplementary Figure 4

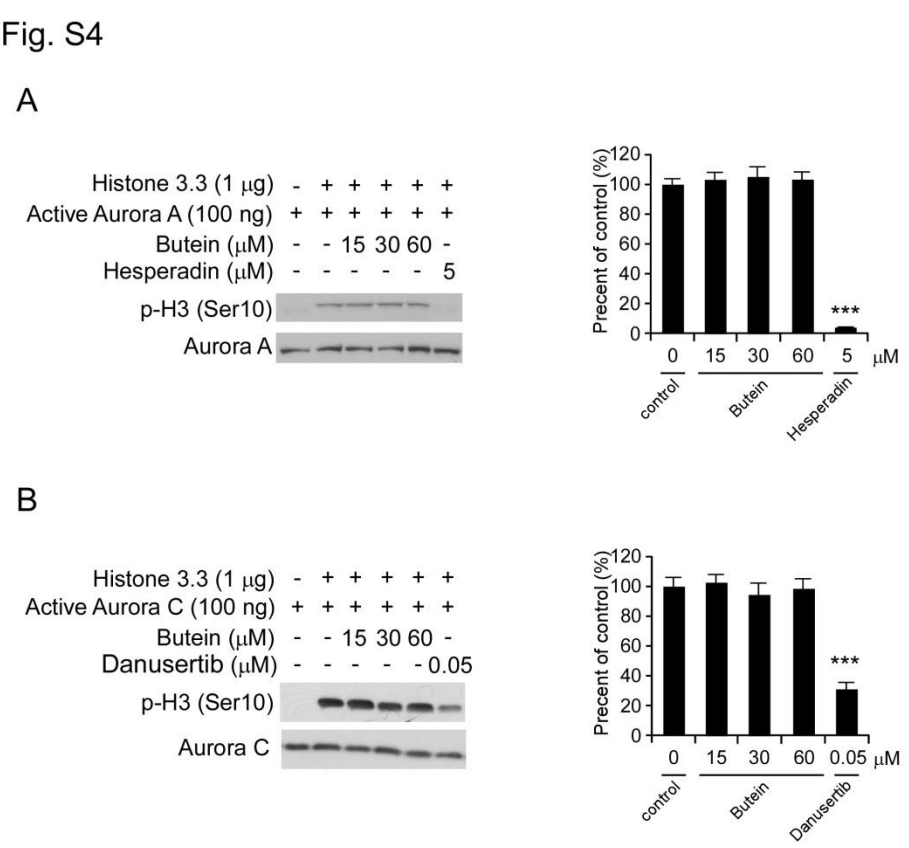
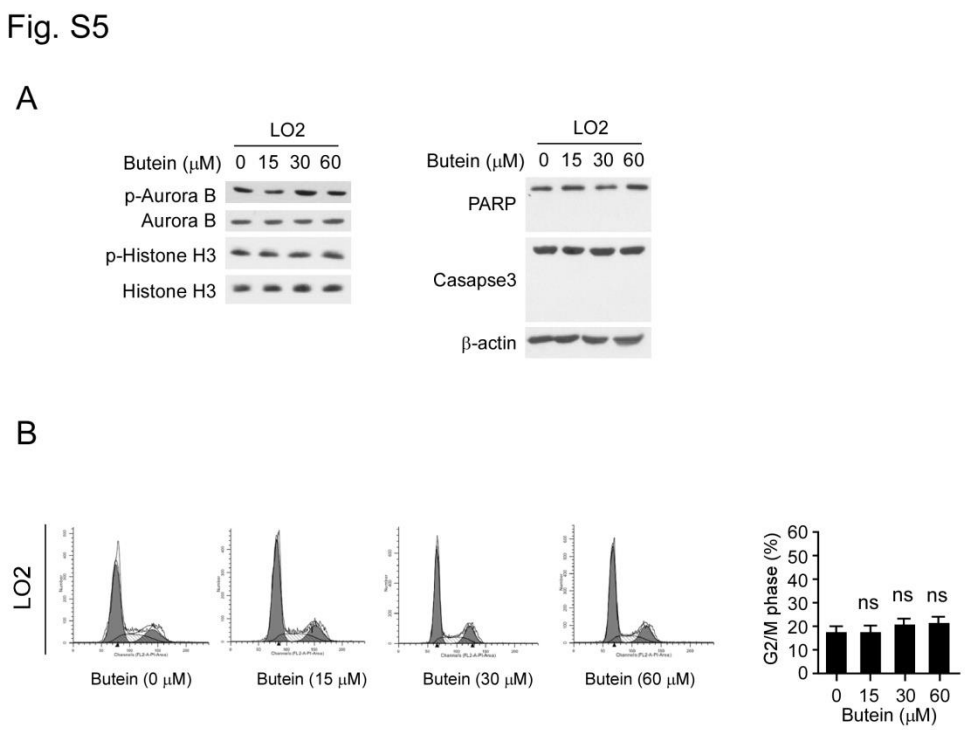


Fig S4. Butein did not inhibit Aurora A kinase activity *in vitro.* Inactive Histone H3.3 protein was incubated with different concentrations of butein, active Aurora A kinase (A) / Aurora C kinase (B) and 100 μM ATP reaction buffer at 30 ^{O}C for 30 min, the phosphorylation of histone H3 was examined by western blotting, Hesperadin/Danusertib was used as positive control. ***, p<0.001.

Supplementary Figure 5



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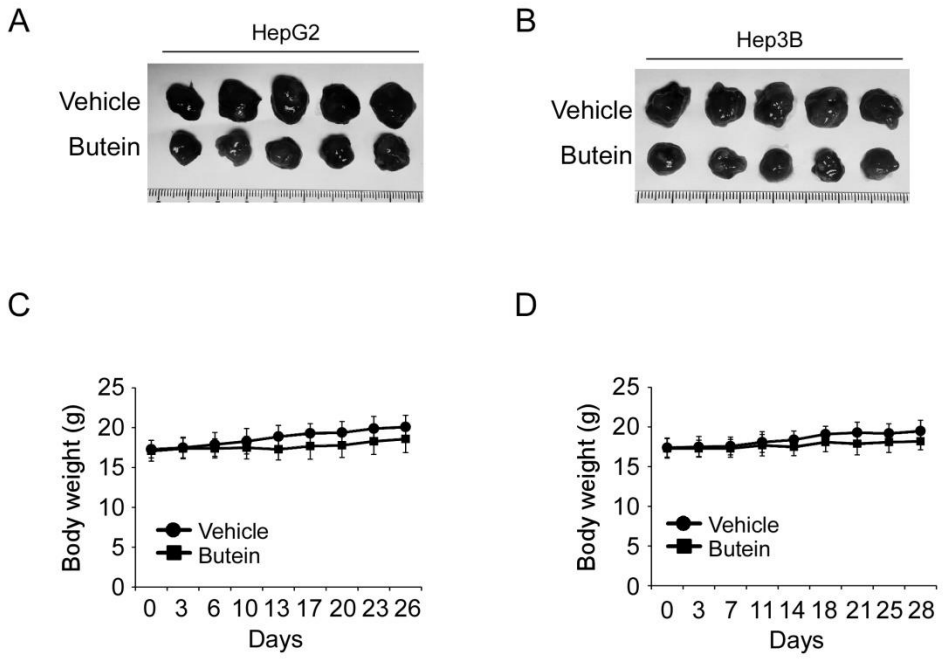
Supplementary Figure 6

Fig. S6



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Supplementary Table 1

Table S1

kinase profiling of Butein

Kinase profiler screening was conducted with 20 μM butein and 10 μM ATP according to Millipore's protocol. Scores are represented as percent (%) of activity remaining after treatment. h, human.

Kinase	Activity	Kinase	Activity
Aurora-A (h)	87	PKBα (h)	87
Aurora-B (h)	29	PKBβ (h)	102
Aurora-C (h)	74	PKCα (h)	82
IKKα (h)	79	PKCδ (h)	78
IKKβ (h)	84	Lck (h)	79
EGFR (h)	39	Lyn (h)	93
Fyn (h)	82	Met (h)	52
GSK3β (h)	98	MSK1 (h)	111
JNK1α1 (h)	109	MSK2 (h)	99
JNK2α1 (h)	88	mTOR (h)	72
JNK3 (h)	98	PDK1 (h)	104
JAK2 (h)	95	PI3 Kinase (p110a/p85a) (h)	97
MEK1 (h)	79		