**Table 1: Contractile responses to S6c and ET-1 in MCA incubated with four different PKC inhibitors**

| | | S6c | | ET-1 | |
|---|---|---|---|---|---|
| | n | Emax (%) | $pEC_{50}$ | Emax (%) | $pEC_{50}$ |
| Control | 10 | 131 ± 7 | 9.13 ± 0.10 | 152 ± 6 | 8.74 ± 0.12 |
| Bisindolylmaleimide I | 14 | 73 ± 8** | 8.97 ± 0.08 | 143 ± 6 | 8.70 ± 0.08 |
| Chelerythrine chloride | 9 | 102 ± 7 | 8.95 ± 0.20 | 139 ± 6 | 8.77 ± 0.18 |
| PKC inhibitor 20–28 | 14 | 67 ± 10** | 8.80 ± 0.16 | 145 ± 7 | 8.64 ± 0.17 |
| Ro-32-0432 | 9 | 6 ± 3*** | 8.92 ± 0.07*** | 194 ± 12 | 8.36 ± 0.09 |

*P < 0.05, **P < 0.01, ***P < 0.001 compared to control. *n* represents the number of artery segments.

### *PKC subtype expression*

Western blot experiments were carried out using antibodies directed specifically against phosphorylated, and thereby activated, PKC isoforms (α, βI, γ, δ and ε). These tests showed that PKCi 20–28 was able to decrease the protein amount of all five PKC subtypes tested, although the decrease was most prominent for PKCδ (38% ± 20% of control, Fig. 4A) and PKCγ (51% ± 36% of control, Fig. 4B). Conversely Ro-32-0432 and Bis I did not decrease the protein levels of the PKC subtypes.

## Discussion

This study shows that each of the three general PKC inhibitors attenuates the organ culture induced upregulation of the $ET_B$ receptor mediated contraction seen in rat MCA. A fourth PKC inhibitor, chelerythrine chloride, had no effect on the contractile responses of the arteries, and consequently was not included in the additional experiments. A possible explanation to this lack of effect could be that chelerythrine chloride has been shown to alter vasoconstrictive responses through interaction with various phos-

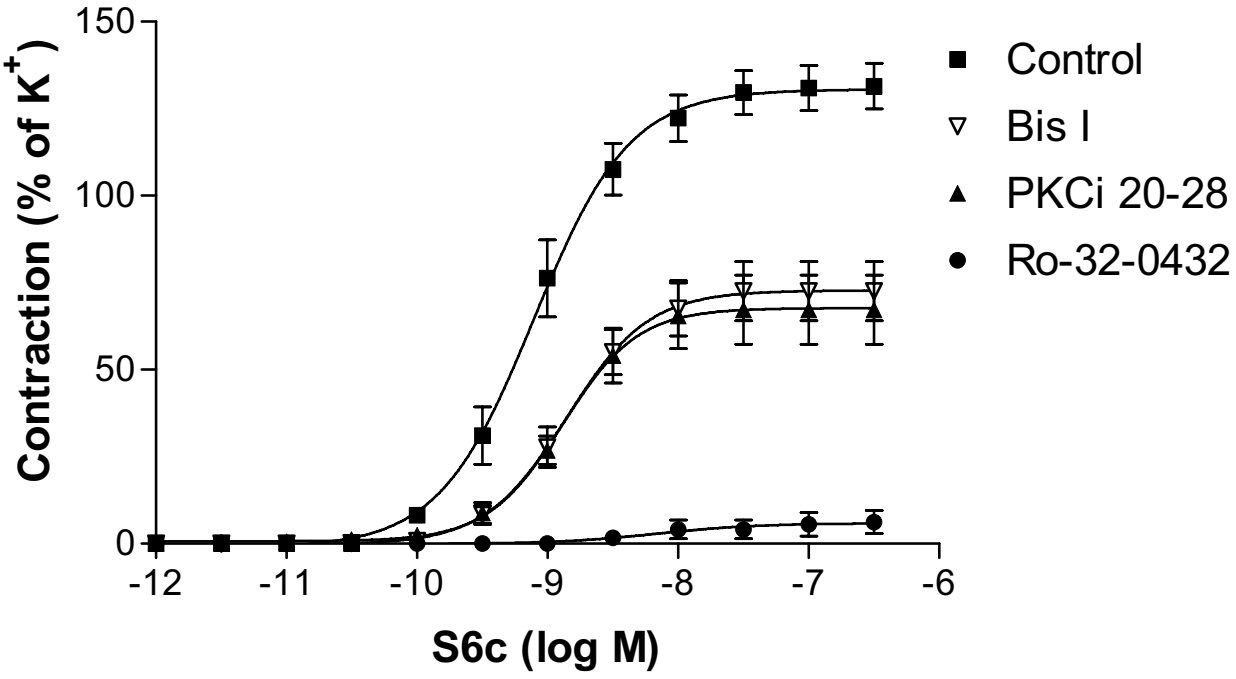


**Figure 1**

**Contractile response towards S6c**. Contractile responses towards the $ET_B$ receptor agonist S6c in MCAs incubated for 24 hours (control) and MCAs incubated for 24 hours with PKC inhibitors (Bis I, Ro-32-0432, PKCi 20–28). Each point represents mean value ± S.E.M. For statistical analysis, see Table 1.