Ovariectomy decreases the responsiveness to estrogenic compounds of creatine kinase specific activity in aorta and left myocardial ventricle.

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Ovariectomy of immature female rats, results in significant decreased metabolic activities in various organs due to decreased estrogen levels which can be restored by estradiol-17β (E_2) and a variety of phytoestrogens. In the present study, we compared the effects of E_2 to those of the phytoestrogens: quercertin (Qu), daidzein (D), genistein (G), biochainin A (BA) and their carboxy-derivatives cD, cG and cBA in aorta (Ao) and left ventricule of the heart (Lv) in immature and Ovx female rats, on creatine kinase specific activity (CK; a hormonal responsiveness marker), when injected for 24h with and without the SERM raloxifene (Ral) or with and without pre-treatment for 3 days with the less-calcemic vitamin D analog JKF 1624 F_2-2 (JKF). We found that: 1) Ovariectomy resulted in significantly reduced basal level of CK in Ao by 47% and in Lv by 36%. 2) All estrogenic compounds tested in both types of rats stimulated CK. 3) In Ao and in Lv some of the estrogenic compounds were significantly more effective in immature rats than in Ovx. This might be due to decreased estrogenic sensitivity in ovariectomy. 3) The SERM Ral inhibited estrogenic stimulated CK in a less effective pattern in Ovx than in immature rats. 4) In Lv on the other hand Ral was similarly effective in both animal types. This different in responsiveness to Ral might be due to different effects of estrogen removal to the level and activity of the different estrogen receptors (ERs). 5) In Ao pre-treatment with JKF decreased CK response to the different estrogenic compounds whereas in Lv this pre-treatment increased CK only by E2, G and D in both animal types. This might be due to the different effects of JKF on ERs in both organs leading to altered estrogenic responsiveness. In summary, the estrogenic response of vascular female rats organs are modulated by ovariectomy in an organ- and substrate-

dependent manner which might be correlated with the modulation of the level and/or the binding activity of the different ERs due to the decrease in circulating estrogen.

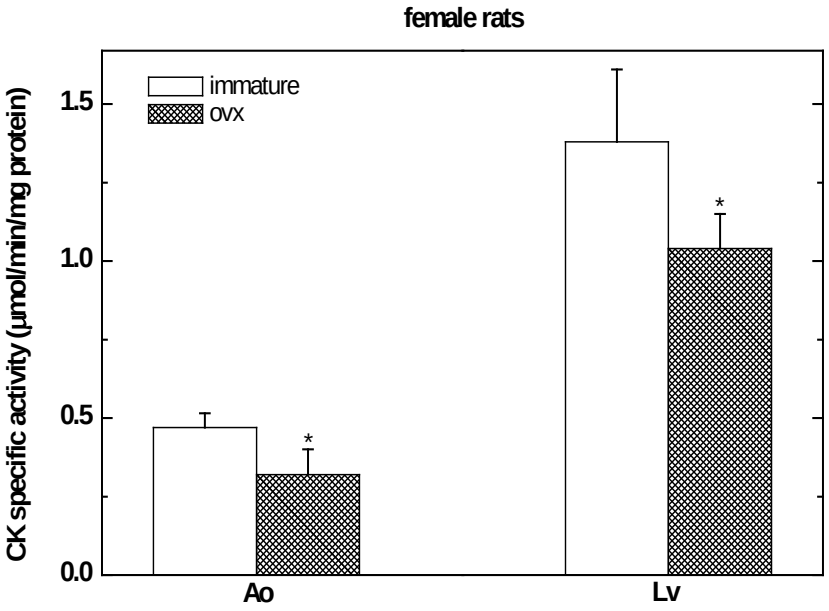


Fig 1

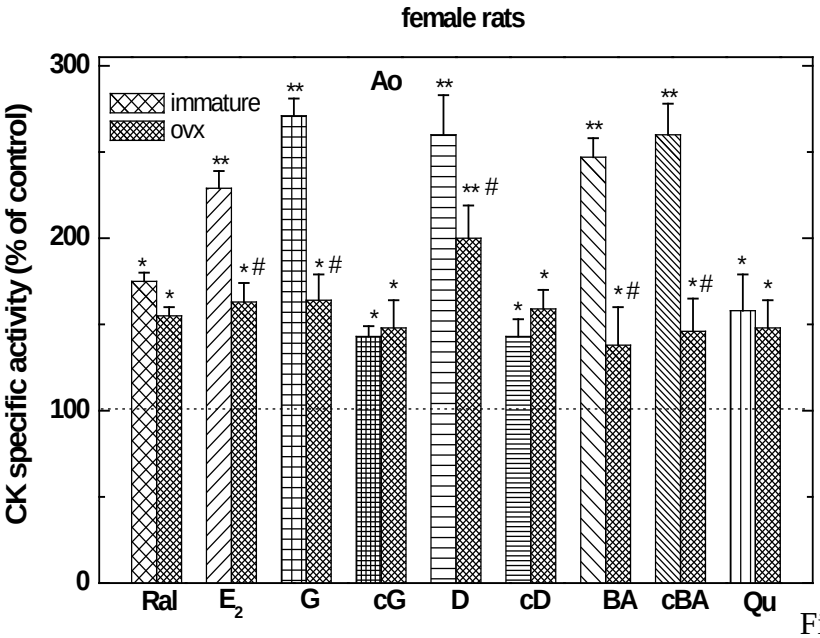

female rats
Ao
immature
ovx
CK specific activity (% of control)
300
200
100
0
Ral
E2
G
cG
D
cD
BA
cBA
Qu

Fig 2a

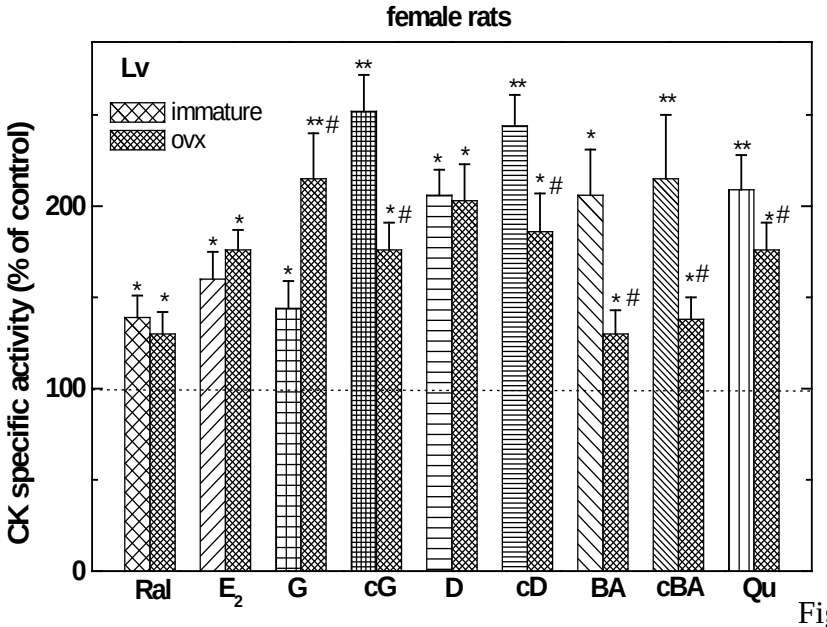
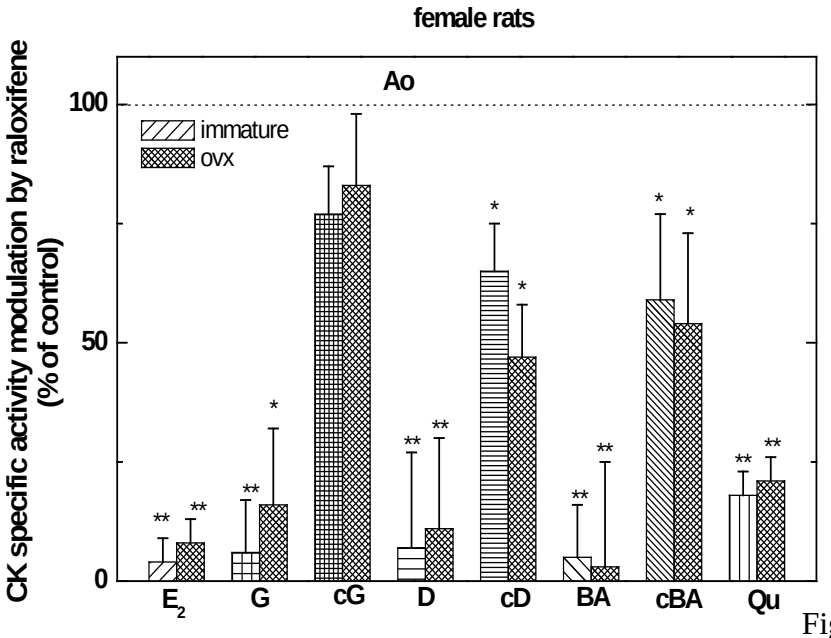

female rats
Lv
immature
ovx
CK specific activity (% of control)
0
100
200
Ral
E2
G
cG
D
cD
BA
cBA
Qu

Fig 2b


female rats
Ao
CK specific activity modulation by raloxifene
(% of control)
100
50
0
immature
ovx
**
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*
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*
*
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*
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**
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E2
G
cG
D
cD
BA
cBA
Qu

Fig 3a

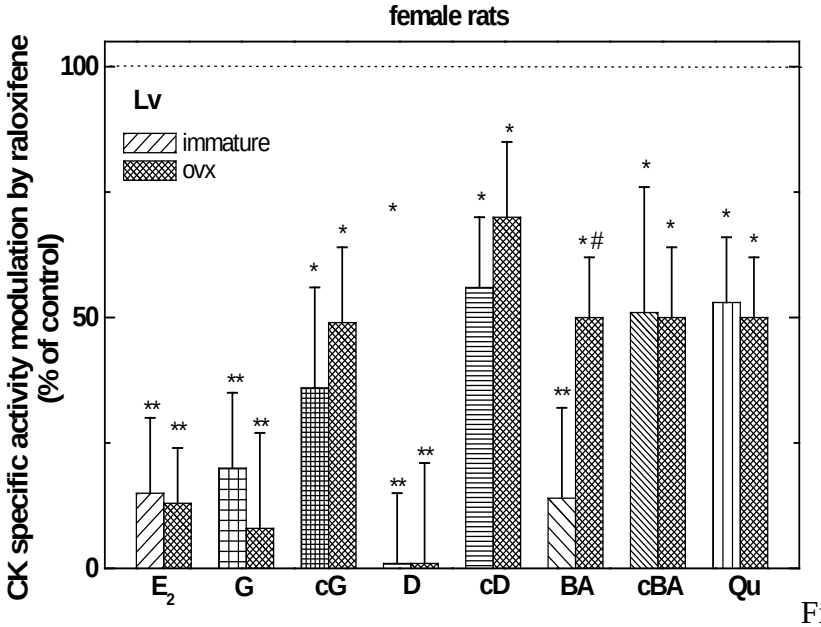
female rats
CK specific activity modulation by raloxifene (% of control)
100
50
0
Lv
immature
ovx
E2
G
cG
D
cD
BA
cBA
Qu

Fig 3b

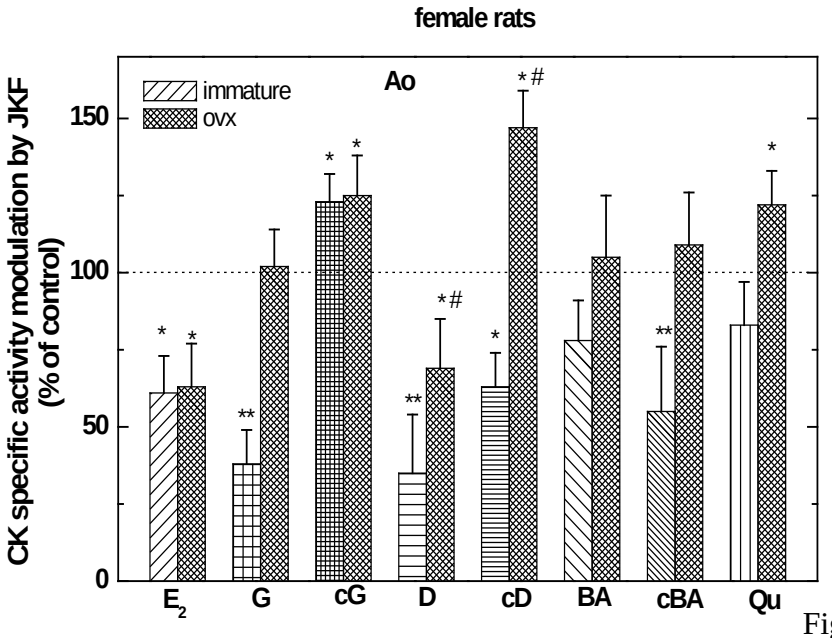
female rats
Ao
immature
ovx
CK specific activity modulation by JKF
(% of control)
150
100
50
0
E2
G
cG
D
cD
BA
cBA
Qu

Fig 4a

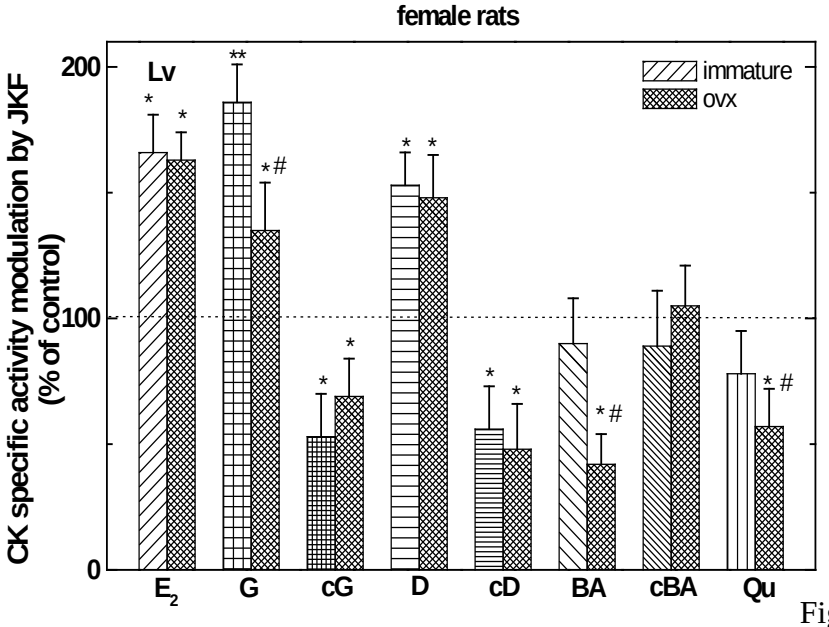
female rats
CK specific activity modulation by JKF
(% of control)
200
100
0
Lv
immature
ovx
E2
G
cG
D
cD
BA
cBA
Qu

Fig 4b