

# Search of natural compounds that modulate the concentration of intracellular calcium ions

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## Editorial

Calcium is a highly positively charged ionic species and play an important role in the metabolism and physiology of eukaryotes.<sup>1-3</sup> It forms a gradient across the plasma membrane, with extracellular concentrations being about 10,000 times higher than intracellular ones.<sup>4,5</sup> Inside the cell, calcium concentrations can vary between different organelles, and the transport of calcium between the cytoplasm and organelles such as the sarcoplasmic (SR) and endoplasmic reticulum (ER) acting to control cytosolic calcium concentrations.<sup>1,3,6,7</sup> Signalling events (or drug actions) often involve an influx of calcium across the plasma membrane, or release of calcium from the SR/ER, where the increase in cytosolic calcium can initiate or alter cellular processes. A whole range of cellular processes is regulated by the free cytosolic calcium concentration, ranging from transcription control and cell survival to neurotransmitter release and muscle function.<sup>1,7-10</sup> In order for a cell to use calcium as a signalling molecule, the cell must create calcium gradients across membranes. To obtain such concentration differences, calcium ions need to be actively pumped across membranes against a concentration gradient. Cells use calcium pumps to direct the flow of calcium ions through the plasma membrane or organelle membranes, and the resulting gradients are used in a variety of signalling systems mediated by gated ion channels. Calcium pumps are ATPases that transport ions across membranes using energy obtained from the hydrolysis of ATP.<sup>11-13</sup>

The SR/ER plays an important role in regulating cytosolic calcium levels through SERCA pumps, which accumulate calcium in the SR/ER lumen. The mobilization of calcium from intracellular organelles is highly specialized in cardiac and skeletal muscle. In skeletal muscle, calcium ions are transported against a concentration gradient from the cytoplasm into the SR, which causes the relaxation of muscle cells following the excitatory effect of high cytosolic calcium. In cardiac muscle, the control of intracellular calcium is essential for the regulation of cardiac contractility, and relies upon SERCA and PMCA pumps.<sup>2,4,14-16</sup>

It is quite easy to prepare SR/ER membranes using ultracentrifuge especially from skeletal muscle (3-6). The Ca<sup>++</sup>-ATP activity can be measured using spectrophotometric method while the up-take and release of Calcium can be determined by spectrofluorimetric method.<sup>3,5</sup> The activity of Ca<sup>++</sup>-ATPase can be measured in the presence and absence of unknown compound<sup>3-5,8,9</sup> and the effects of that compound can be calculated easily. The search of new natural compounds that regulate this ATPase may be more valuable for the developing countries which have too many unexplored natural resources, especially plants.<sup>17,18</sup> One of the major precautions must be kept in mind that the isolated component must be free of any intrinsic calcium.

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## Conflicts of interest

The authors declare that there are no conflicts of interest.

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