

As an alternative, blood pressure monitoring equipment capable of transmitting data over radio frequencies can be surgically implanted into various animal species. In this case, training the animals to tolerate the use of a blood pressure cuff is unnecessary, but significant healing time (2–4 weeks) is required in order for the animals to recover from the surgical implantation. After the animals have healed and become acclimated to their surroundings, the radio transmitting equipment allows 24h monitoring of blood pressure in the animals. This telemetry-driven animal system has been successfully employed in a wide range of animal species.²⁹

Once the animals are ready (e.g., trained, healed, acclimated, etc.), dosing with test compound can be initiated. The typical efficacy study for a potential antihypertensive agent will require extended dosing periods (1–2 weeks) during which changes in blood pressure are monitored. Other aspects of cardiovascular performance such as heart rate, contractility, and ejection fraction are often monitored to ensure that the remaining aspects or cardiovascular performance are not negatively impacted. On the whole, testing a potential antihypertensive agent in a suitable animal model can require several weeks, possibly months of effort by the appropriately trained staff, making it very important that only molecules that are properly vetted reach this stage.

Models of Hyperlipidemia and High Cholesterol

It is well established that increased levels of cholesterol (Figure 7.10(a)) and low-density lipoprotein (LDL, Figure 7.10(c)) are associated with significantly increased risk of atherosclerosis and related cardiovascular

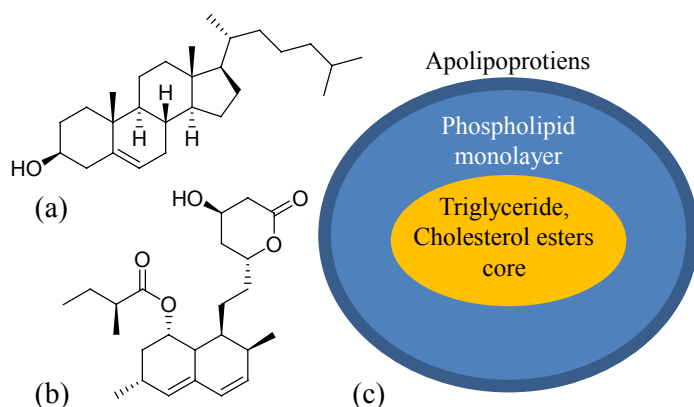


FIGURE 7.10 (a) Cholesterol (b) Mevacor[®] (lovastatin), an HMGCoA reductase inhibitor. (c) Low-density lipoprotein (LDL) particles are composed of a triglyceride and cholesterol ester core surrounded by a phospholipid monolayer. Apolipoproteins are often embedded in the surface of the LDL particle.