Blood is the medium that transports drugs, and it is also the medium from which drug concentrations are measured. One usually cannot monitor a drug at its target, such as tissue from a joint for an arthritis drug or tissue from the brain for a headache reliever. One can, however, easily draw blood from a vein and check the concentration of a drug present in the bloodstream. Presumably, the concentration of the drug is somehow proportional to the concentration of the drug at the target. If that assumption is true (and it generally is), knowing the amount of drug in the blood is just as good as knowing the concentration at the target.

Blood, more specifically **whole blood**, is a complex mixture of water, electrolytes, small organic molecules (e.g., hormones), proteins, and cells. An overall breakdown in shown in the figure below.

When whole blood is sampled from a patient, it is centrifuged so that all the cells can be removed from the fluid fraction of the blood. The fluid fraction of the blood is called **plasma**. Plasma is approximately 54% of the volume of whole blood. Plasma includes water, salts, small molecules, and proteins. Closely related to plasma is **serum**. Serum is the residual fluid left behind after whole blood clots. Serum is approximately equivalent to plasma without the proteins responsible for clotting.

Proteins in the blood can significantly impact a drug. One way is by affecting how a drug is transported and removed from the bloodstream. That aspect of blood proteins will be covered in a web component. The other way blood proteins affect a drug is by making the drug less effective in terms of the drug-target interaction.

Drugs are designed to bind to targets, and sometimes a drug has a difficult time distinguishing a different protein from its intended target. Blood proteins are never far from a drug because the drug hitches a ride on the bloodstream to get to and from its site of action. If a drug is hindered by binding a blood protein, then the concentration of free, unbound drug is lower and less is available to act on the intended target. Therefore, the drug will be less effective.
Most assays for preliminary activity for a molecule are in vitro assays. These biochemical tests are idealized to determine drug-target binding. As a pool of hits is being filtered to determine which will become leads, the same assays may be performed in the presence of 10 to 50% human serum or plasma. The intent of using serum or plasma is to introduce the type of proteins that will be encountered by the lead in a living organism. The activity (as $K_D$, $IC_{50}$, $K_i$, or $EC_{50}$) of a hit is almost always lower when determined in the presence of blood proteins. The activity can even be dramatically lower. Hits that are greatly affected by blood proteins may be downgraded relative to other hits.