method uses normal cells (e.g., Chinese hamster ovary cells (CHO cells)) and is designed to identify compounds that damage chromosomes or the cell division system. When these systems are damaged, membrane bound DNA fragments, referred to as micronuclei, form during the cell division process due to improper migration of chromosomes during mitosis. Morphologically, micronuclei are identical to the main nuclei of a cell, but they are substantially smaller, making them readily identifiable when present. In practice, cells are grown in the presence of candidate compounds for a brief period of time to provide an opportunity for chromosomal damage. Upon completion of this time period, the cytokinesis-blocking agent cytochalasin B (Figure 8.11(a)) is added, causing the accumulation of cells that have completed one nuclear division to become binucleated cells. These cells are then examined and scored for the presence of micronuclei. A "positive" result is indicated when a compound induces a dose dependent increase in the formation of micronuclei in this assay, suggesting that the compound has genotoxic properties.

Examining cells for structural changes in the chromosomes using the Chromosomal Aberration Assay (Figure 8.12)[28] has also proven to be a

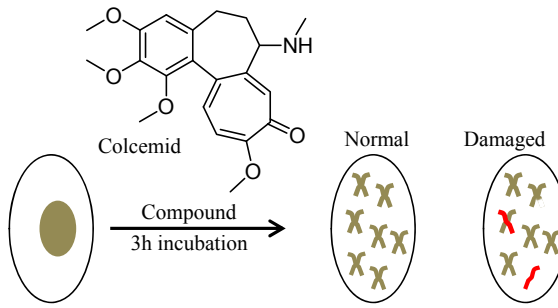

FIGURE 8.12 The chromosomal aberration assay is used to identify compounds that damage genetic material. Incubation of a cell culture in the presence of a candidate compound for a short period of time is followed by the introduction of colcemid. This compound stops the cell cycle at the metaphase, a point at which the condensed and highly coiled chromosomes are aligned in the middle of the cell and visible with a microscope. Cell fixation and microscopic examination provides an opportunity to assess DNA damage that may have been caused by the candidate compound.

useful tool in identifying potentially genotoxic compounds. DNA damage associated with genotoxic compounds can lead to breaks in the chromosomal material (e.g., single and double strand breaks). These breaks can be repaired correctly, rejoined together incorrectly, or not rejoined at all. The first scenario repairs the cell to its normal state, but the second and third scenarios create changes in the overall structure and appearance of chromosomal material that can be observed under a microscope when cells are