permeation flux and lag time of nitroglycerin through rat skin (by two to four times and four times, respectively) when applied with the high-molecular-weight compounds β-cyclodextrin and polyethylene glycol 1540. They attributed the retardation effects of the polymers to reduction of both the diffusion coefficient of nitroglycerin through the skin (possibly due to H-bonding) and its thermodynamic activity in the systems. A similar effect on the flux and lag time of nicotine was shown for different polyethylene glycols and β-cyclodextrin, attributed to either film formation on the skin or complexation with this alkaloid [69]. Other polymers that retard skin permeation include the very hydrophilic and reactive polyanhydride that decreased rat skin permeation of nitrofurazone (by about five times) and nitroglycerin (by about two times), and completely stopped nicotine permeation [70]. The effect on permeation was shown to be affected by the polymer concentration, polymer molecular weight, and type of permeant. Moghimi et al. [71] demonstrated the potential of dendrimers to retard permeation. Generation 5 (G5) polyamidoamine (PAMAM) dendrimer (MW 28800 Da), when applied as either a co-treatment or pretreatment on rat skin, reduced the permeation of furfural (2-furanaldehyde, known to cause contact dermatitis) in a concentration-dependent manner (Figure 17.2). The reduction was attributed to both the chemical interaction between the nucleophilic groups of PAMAM (–NH) and electrophilic group of furfural (COH–) and the physical entrapment of furfural within the dendrimer network.

Another approach is to include chemicals within the formulation that will increase the integrity or reduce the fluidity of the stratum corneum. It has been shown that a chemical that acts as an enhancer can become a retardant, or vice versa, depending upon the vehicle in which it is applied to the skin. For example, Kaushik et al. [72] studied the permeation of the insect repellent diethyl-m-toluamide (DEET) in the presence of laurocapram and iminosulfurane analogues from different

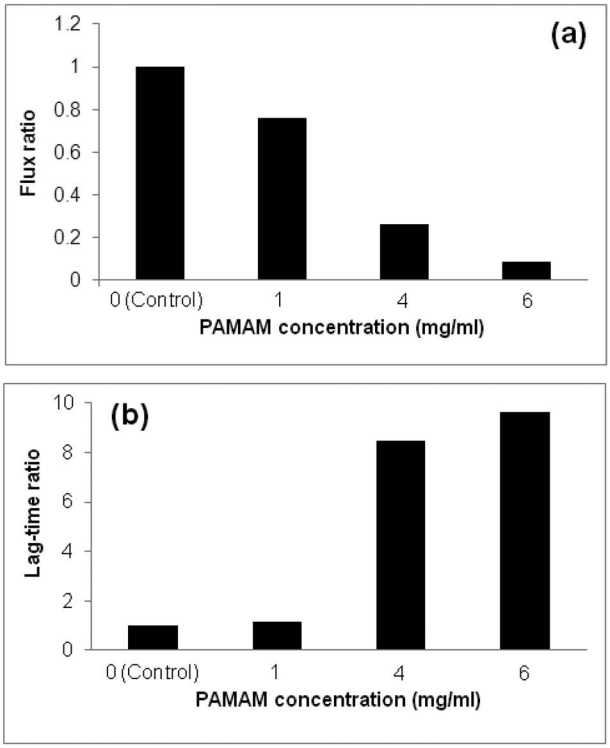

FIGURE 17.2 Retardation effects of PAMAM dendrimer toward permeation of furfural through rat skin, resulting in reduction of flux (a) and elongation of lag time (b). Ratios are PAMAM-treated over untreated values. (Graphs are drawn from raw data published by Moghimi et al. 71.)