and considerable increase in culture volume, but the volume of the workable supernatant (approximately 7 L after biomass removal) hardly changed during the fermentation process (Figure 3). Since a high percentage of the culture is biomass, the appropriate way to express angiostatin production is in mg per liter supernatant instead of mg per liter culture, the average production (based on five consecutive runs) was 20 (+–5) mg L supernatant. Inducing the culture at higher cell densities resulted in significant problems with maintaining the desired temperature and dissolved oxygen level because the high amounts of oxygen, needed for methanol oxidation, generate a large amount of heat during the exponential growth phase on methanol. When the culture density reached approximately 150 OD at 600 nm (10% v/v), about 20 h after starting the fermentation, methanol addition was commenced and its concentration in the culture was kept at 2 g L −1 using the described methanol sensor.