Microbial fuel cells (MFC) have recently received increasing attention due to their promising potential in sustainable wastewater treatment and contaminant removal. In general, contaminants can be removed either as an electron donor via microbial catalyzed oxidization at the anode or removed at the cathode as electron acceptors through reduction. Some contaminants can also function as electron mediators at the anode or cathode. While previous studies have done a thorough assessment of electron donors, cathodic electron acceptors and mediators have not been as well described. Oxygen is widely used as an electron acceptor due to its high oxidation potential and ready availability. Recent studies, however, have begun to assess the use of different electron acceptors because of the (1) diversity of redox potential, (2) needs of alternative and more efficient cathode reaction, and (3) expanding of MFC based technologies in different areas. The aim of this review was to evaluate the performance and applicability of various electron acceptors and mediators used in MFCs. This review also evaluated the corresponding performance, advantages and disadvantages, and future potential applications of select electron acceptors (e.g., nitrate, iron, copper, perchlorate) and mediators.