用いた実験で，AV，SV 及び CV の acid 型がグルクロン酸抱合化を受けること，グルクロン酸抱合化の薬物動態パラメータは動物種間（ヒト，イヌ，ラット），スタチンの種類により著しく異なることを示した．また、ヒト肝ミクロソームを用いた実験で，gemfibrozil は AV acid や SV acid に比べ，CV acid のグルクロン酸抱合化を強く抑制することを示し，これが CV と gemfibrozil との併用による副作用発現頻度増加の原因の一つと推定した．一方，Shitara らは，CV と gemfibrozil との相互作用の機序として，gemfibrozil 及びその代謝物（グルクロン酸抱合体）による CYP2C8 の阻害とともに，OATP2 の阻害を挙げている [104]．CYP2C8 により代謝を受けない PV や PI も gemfibrozil と弱いながら相互作用を示すことは，OATP2 の阻害による寄与を示唆していると考えられる．これまで、一般的には，スタチンは PV を除いて CYP により代謝された後主に胆汁中に排泄されると考えられており，スタチンのグルクロン酸抱合化の重要性についての研究や議論はあまり行われていなかった．また，Prueksaritanont ら(2002) [105]の研究では acid 型のグルクロン酸抱合化の測定のみで，それらの代謝物の抱合化については検討されておらず，メカニズム面を含め，さらに詳細な研究が必要である．

おわりに

スタチンと他の薬剤との相互作用に関して，非臨床，臨床ともに近年著しく研究が進展し，多くの報告がなされてきた．今回の検討では，従来検討されてきた第１相代謝酵素である

CYP 系に加え，トランスポータの寄与について，現時点での知見をとりまとめたが，相互作用へ影響を与える要因として，血中蛋白結合率，初回通過効果，脂溶性，acid 型と lactone 型との変換などの要素に関する研究も必要と考えられる．開発に当たって、臨床現場で使用されうるすべての医薬品との臨床上の相互作用試験を行うことは現実的でないが，起こりうる相互作用を予測し，副作用を未然に防止するためには，代表的な薬剤との臨床相互作用研究の蓄積も必要であると考えられる．

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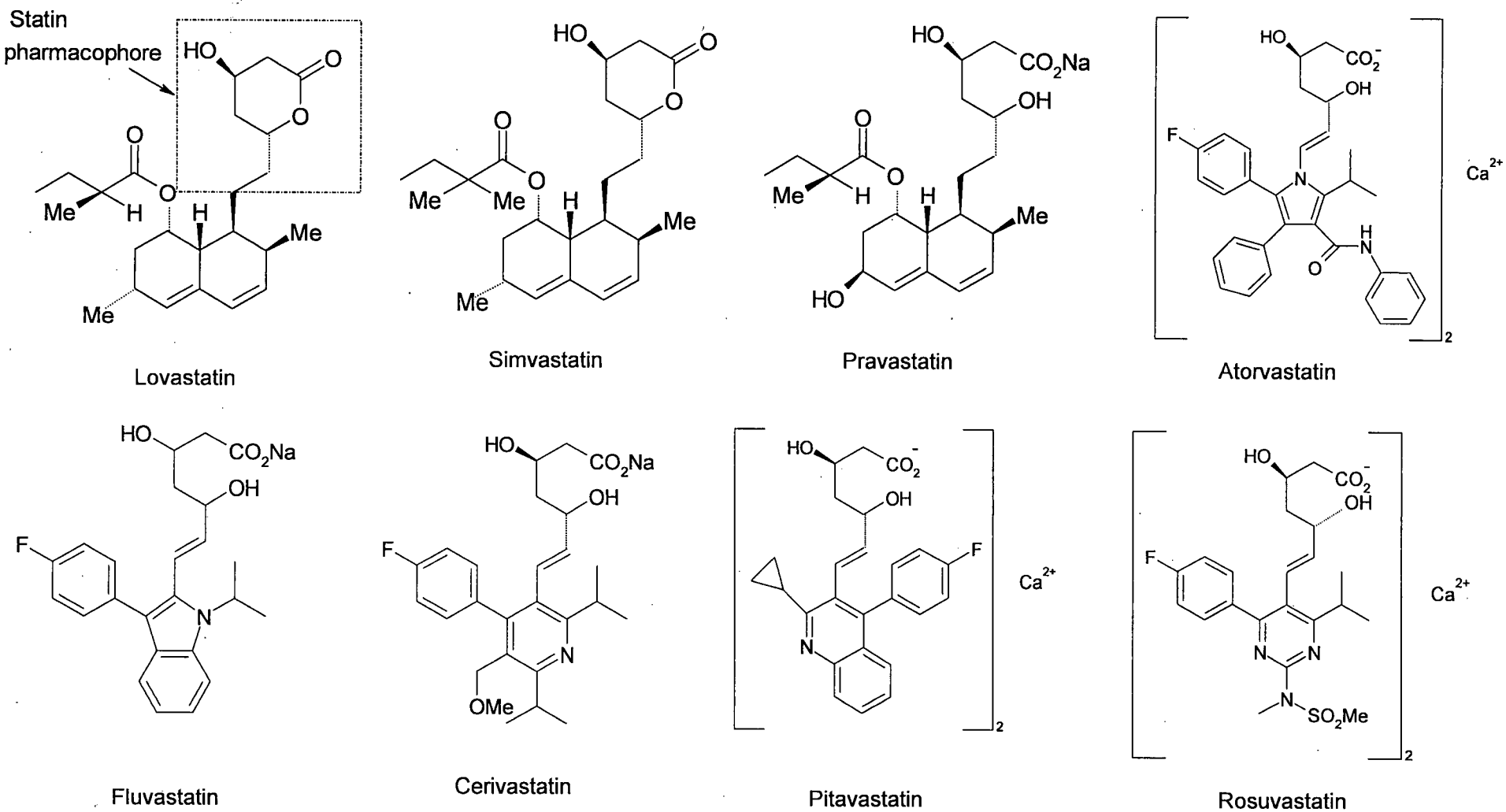

Fig. 1 Chemical Structures of Statins