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TABLE 1. Pharmacokinetic parameters of thiazolidinediones

Parameter	Troglitazone (1997-2000)*	Rosiglitazone (1999-present)*	Pioglitazone (1999-present)*
Oral dosage (mg/day)	200-600	1-8	15-45
Plasma protein binding	> 99%	99.8%	> 99%
Absolute bioavailability	40-50%	99%	83%
C_{max} (μg/ml)	0.90-2.82	0.076-0.598	$1.4 \pm 0.2^{+}$
AUC (μg-h/ml)	7.4-22.1	0.358-2.971	$11.6 \pm 2.2^{+}$
t_{max} (h)	< 2-3	1.75	< 2
Plasma elimination half-life (h)	16-34	3-4	3-7
Biliary excretion	85%	23%	NA^{++}
Urinary excretion	3%	64%	15-30%
Effects of food	Increases the extent of absorption by 30% to 80%	Decrease in C_{max} by 28% and delay in t_{max}	Slightly delay in t_{max} to 3-4 h

* Year on clinical application

$^{+}$ For 30 mg/day oral dosage (Data from the product leaflet of Actos®, Takeda Pharmaceutical Co. Ltd., Japan)

$^{++}$ Most of the oral dose is excreted into the bile

Figure Legends

Fig. 1. Structures of thiazolidinediones and pathways of troglitazone metabolism.

Fig. 2. Reactive metabolites of troglitazone catalyzed by CYP3A.

Fig. 3. Schematic representation of the effects of troglitazone in liver cells.

Fig. 1. Maniratanachote and Yokoi

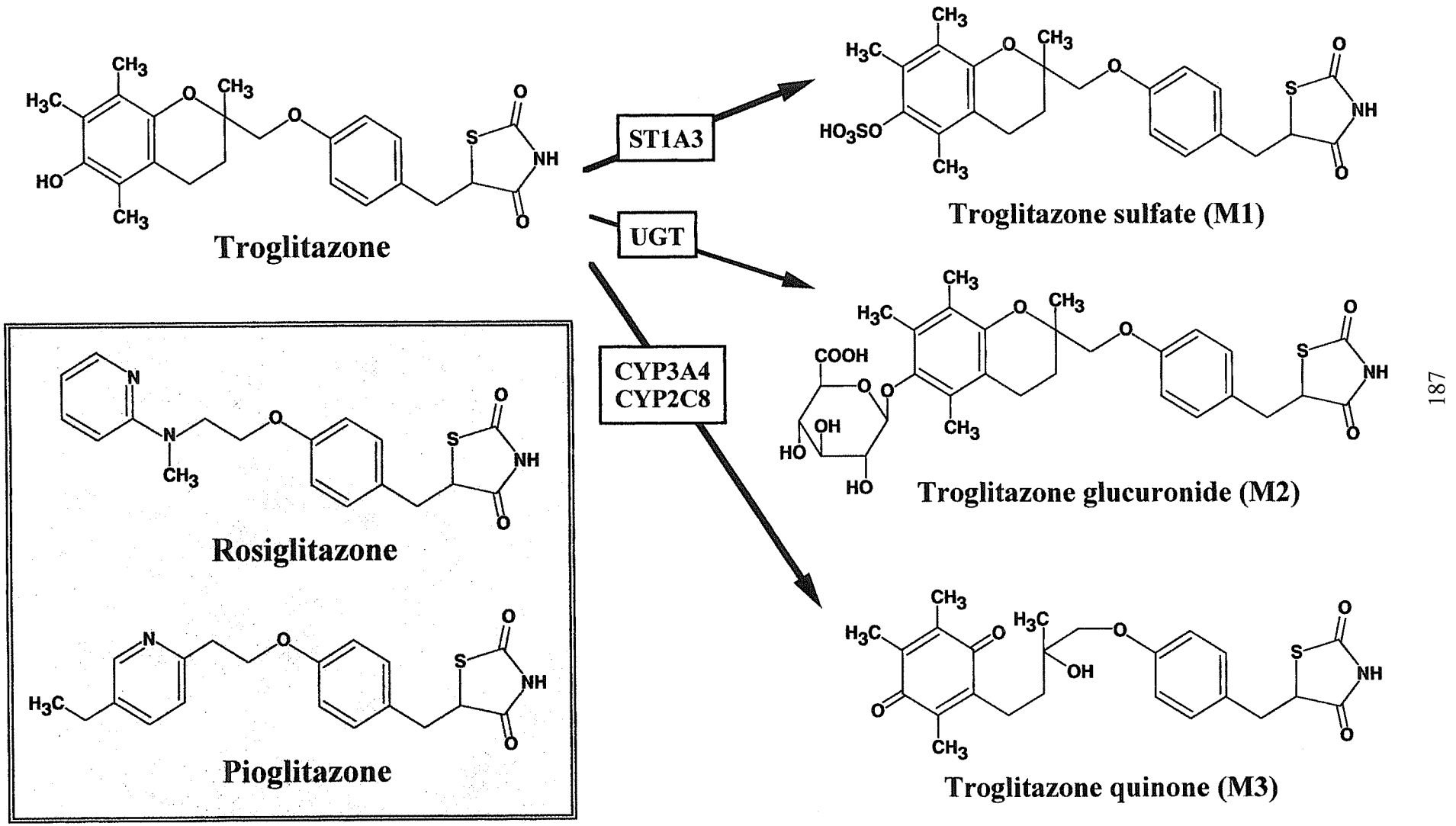
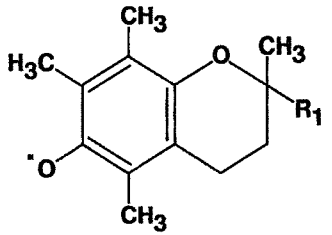
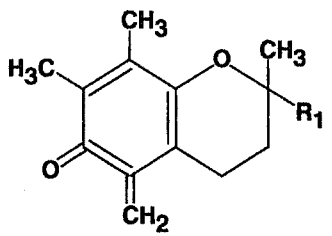


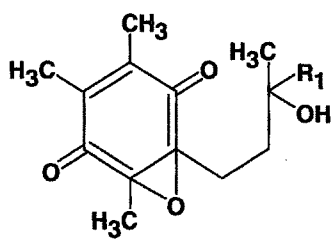
Fig. 2. Maniratanachote and Yokoi



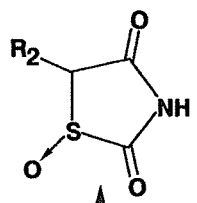
Phenoxy redical intermediate

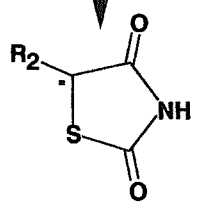


***o*-Quinone methide**

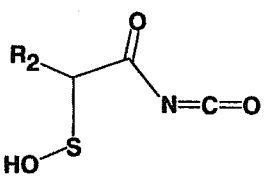


Quinone epoxide





Sulfoxide intermediate and radical



α-Ketoisocyanate derivative

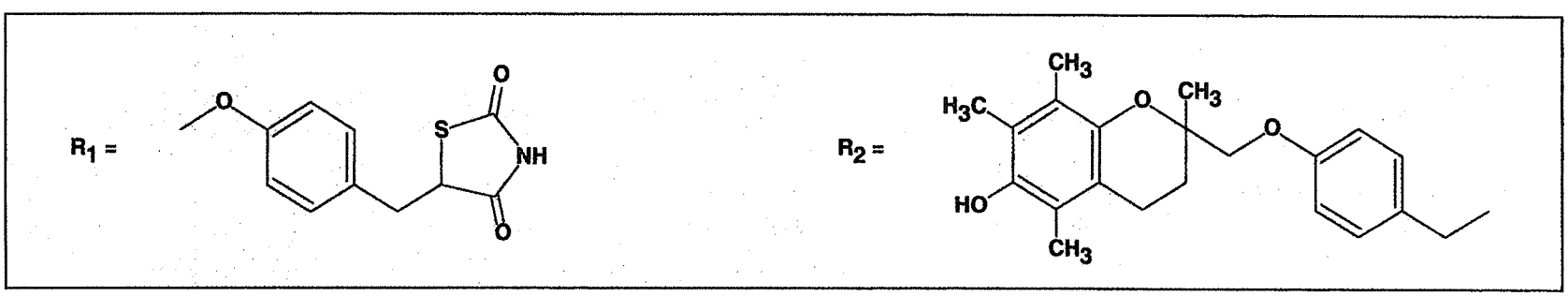


Fig. 3. Maniratanachote and Yokoi