

# THE EFFECT OF ONCE DAILY MELOXICAM ON ANTIPLATELET EFFECT OF LOW DOSE ACETOSAL ON HEALTHY SUBJECTS

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## BACKGROUND

- **Low dose acetosal** is used widely for patients with myocardial infarct, angina, stroke, and peripheral vascular diseases.
- Acetosal is a **first line therapy** which efficacy has been proven, affordable, and oftenly prescribed in Bag./SMF of RSU Dr. Soetomo.
- Low dose acetosal is generally used on a **long term bases**
- Acetosal **suppresses COX-1** in platelet (which main product is Thromboxane/TXA<sub>2</sub>)

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- Patients who take low dose acetosal may also experience **pain and inflammation** in various causes, that may require **NSAID**.
- Meloxicam is also oftenly prescribed **in poli geriatry** of Dr. Soetomo Teaching Hospital , mostly, indicated for osteoarthritis
- Meloxicam **suppresses COX-2** in endothel ( which main product is prostacycline/PGI<sub>2</sub>)
- Meloxicam is a **COX-2 preferential inhibitor**, so it has lighter side effects than other NSAIDs

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## OBJECTIVE

- To find out whether concomitant use of meloxicam, a COX-2 inhibitor, significantly decreases anti-aggregation effect of low dose acetosal, using *Platelet Aggregation Profiler* (PAP-4D).

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## Hypothesis

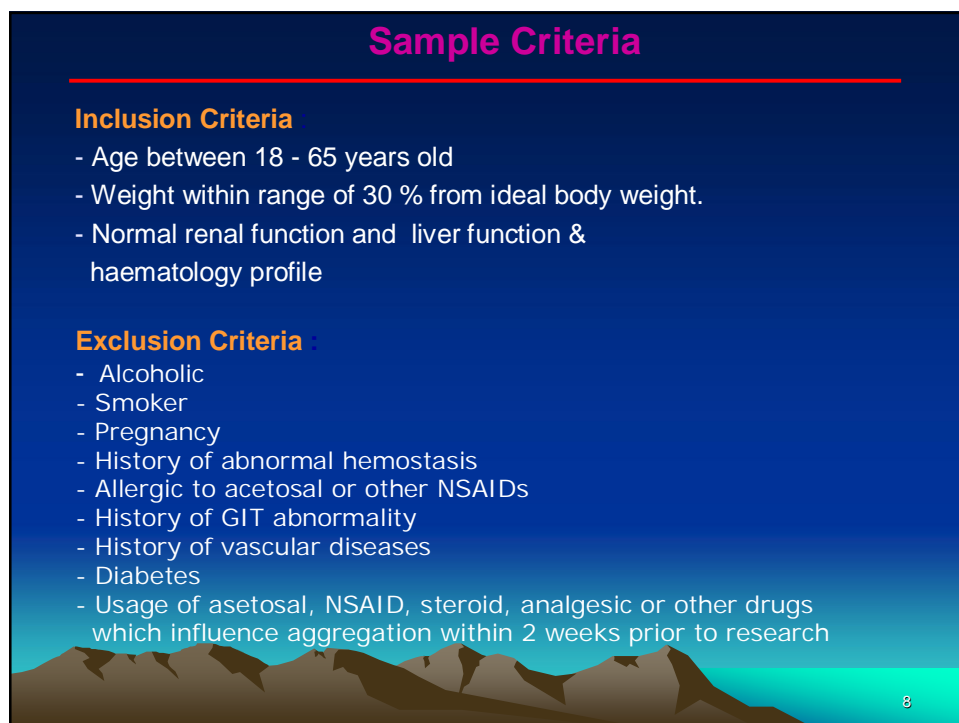
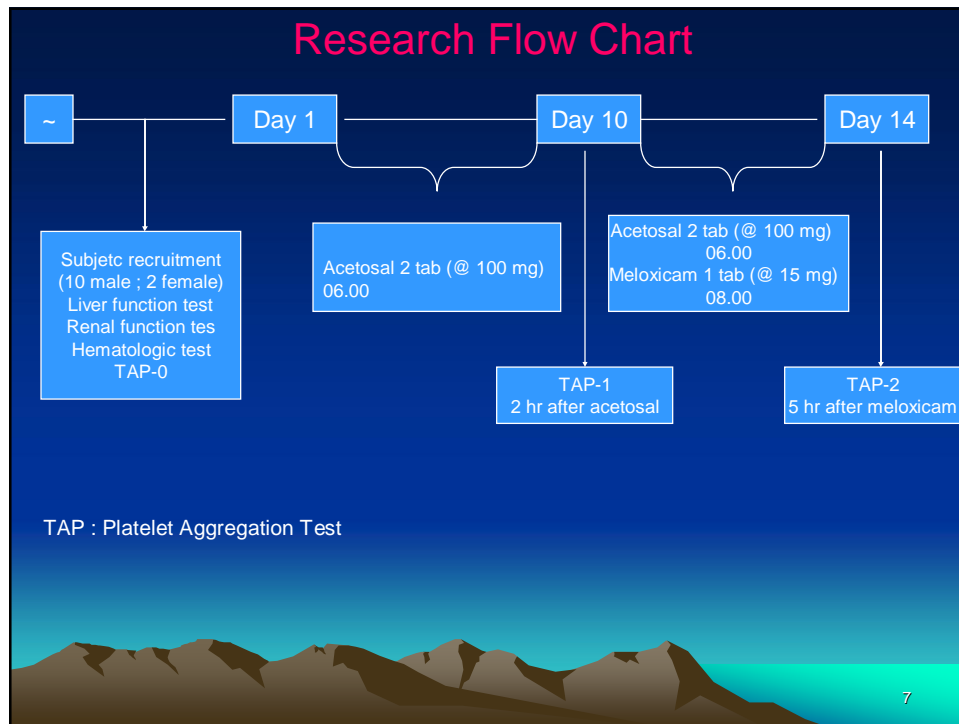
Meloxicam will influence acetosal activity by disrupting the balance between TXA2 and PGI2

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## Material and Methods

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## Instrument

### Platelet Aggregation Profiler PAP-4D



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## Data Analysis

Data from Platelet Aggregation Tests (TAP in Indonesia) with various inductors :

(TAP-0) is base line aggregation,

(TAP-1) is aggregation after taking acetosal for 10 days,

and (TAP-2) is aggregation after taking combination of acetosal and meloxicam for 5 days

are then analyzed statistically using paired samples t-test.

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# Result

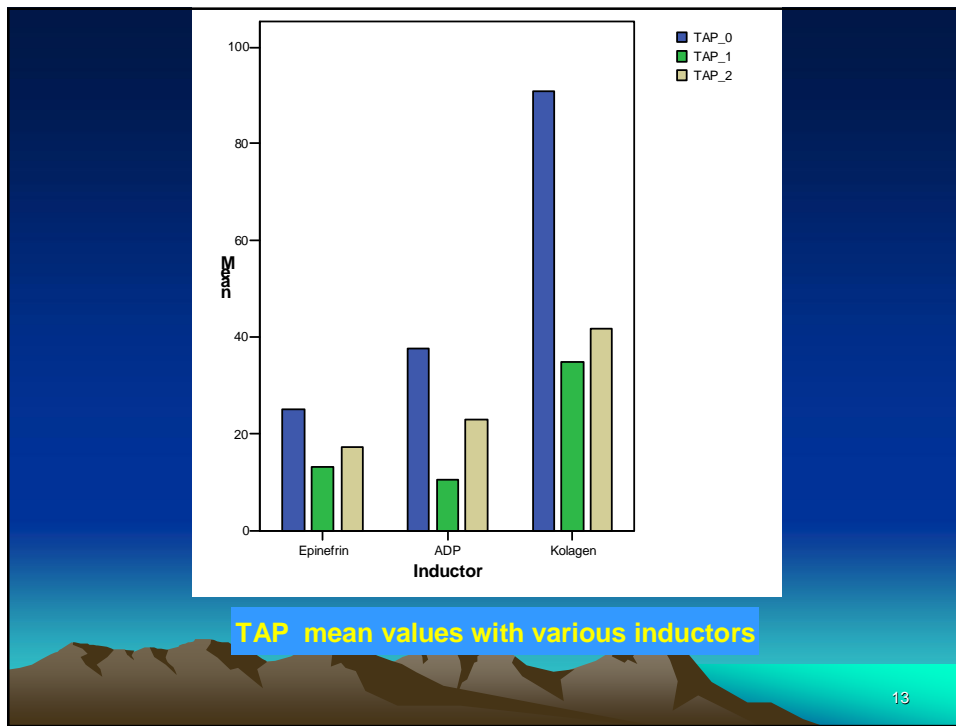
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Table : mean TAP values with various inductors

	Inductor					
	Epinephrin		ADP		Collagen	
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
TAP_0	26	19	38	34	89	25
TAP_1	14	9	11	10	41	25
TAP_2	17	10	25	23	44	33

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### Paired Samples t-Test Result

Inductor	Pair	t test	t table	Sig	$\alpha$	Decision
Epinephrine	TAP-0 & TAP-1	2.020	2.2010	0.0068	0.025	No sig diff
Epinephrine	TAP-1 & TAP-2	-1.023	2.2010	0.328	0.025	No sig diff
ADP	TAP-0 & TAP-1	3.293	2.2010	0.003	0.025	Sig diff
ADP	TAP-1 & TAP-2	-2.017	2.2010	0.059	0.025	No sig diff
Colagen	TAP-0 & TAP-1	6.569	2.2010	0.001	0.025	Sig diff
Colagen	TAP-1 & TAP-2	-7.08	2.2010	0.493	0.025	No sig diff

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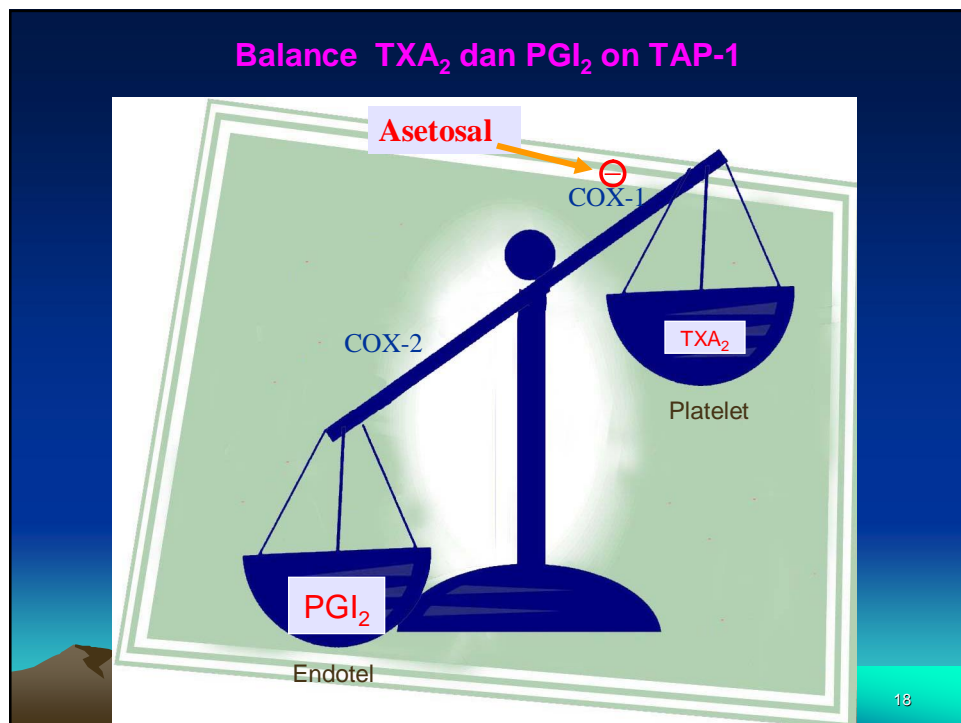
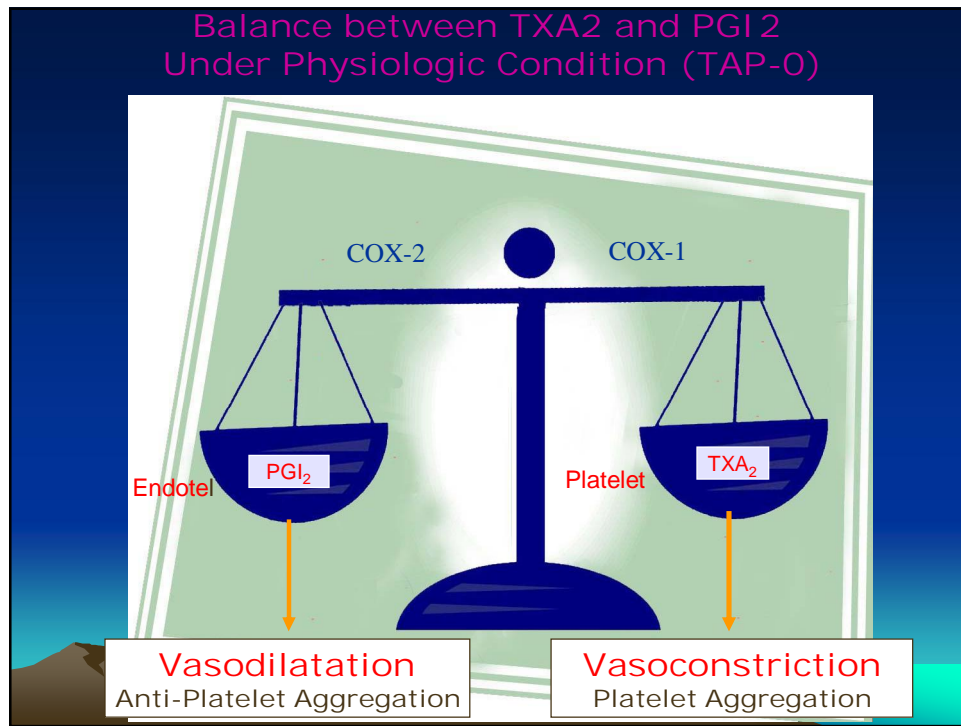
# DISCUSSION

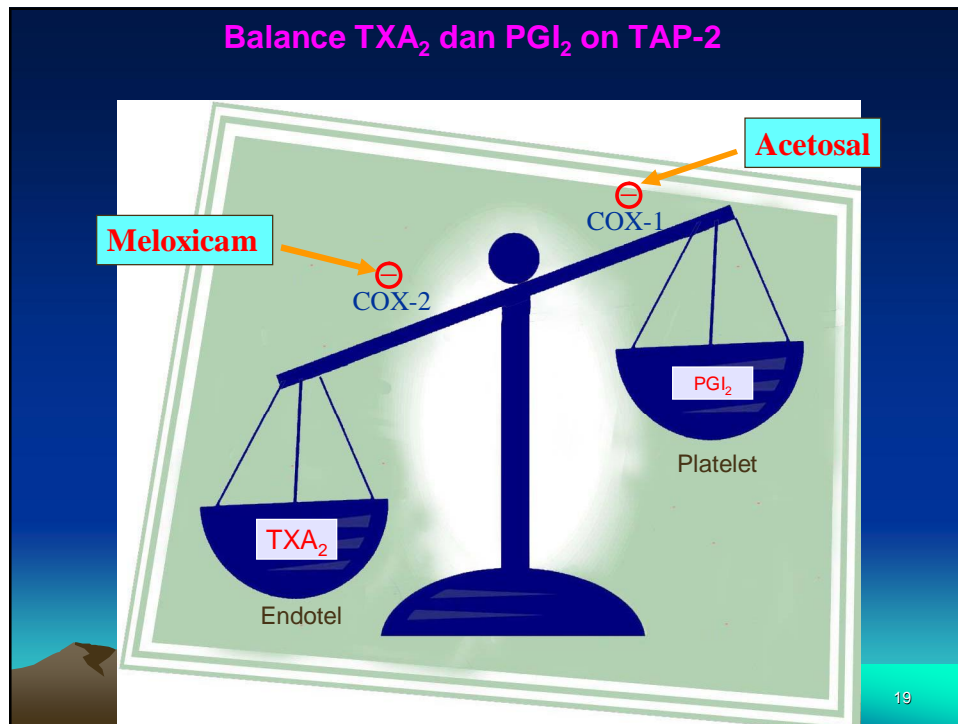
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## Study Design Rationale

- Acetosal was given for 10 days before giving combination treatment  
Platelet's COX-1 inhibition by acetosal is completed (> 95 %) within 7-10 days
- Sampling for TAP-1 was done 2 hours after taking acetosal.  
Acetosal effect can be observed not less than 1 hour after ingestion
- Meloxicam was taken 2 hour after asetosal ingestion  
To give the oppotunity for acetosal to interact with serin 529
- Acetosal and meloxicam combination was given for 5 successive days  
Meloxicam steady state is reached within 4-5 days
- Sampling for TAP-2 was done 5 hours after taking meloxicam  
Meloxicam peak concentration is reached within 5-6 hours

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- Comparison between TAP-0 and TAP-1 with epinephrine as inductor should have resulted significant difference like other inductors, otherwise we couldn't be sure whether acetosal was indeed effective in particular subjects
- But it didn't, this is because epinephrine result is highly variable depending on physical activity and mental status of the subjects

## Conclusion

- Once daily dose meloxicam does not significantly effects on anti-platelet effect of low dose acetosal

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## SUGGESTION

- We hope the same research can be done to patients with atherosclerosis because it will be a very valuable continuation to this study
- In atherosclerotic blood vessel, TXA<sub>2</sub> and PGI<sub>2</sub> production both increase, partly due to enhancement of COX-2 induction in atherosclerotic plaque as well as COX-1 in platelet and other tissues. This state of balance is completely different than those of normal healthy person, and patients with this condition are the ones acetosal is mainly indicated for

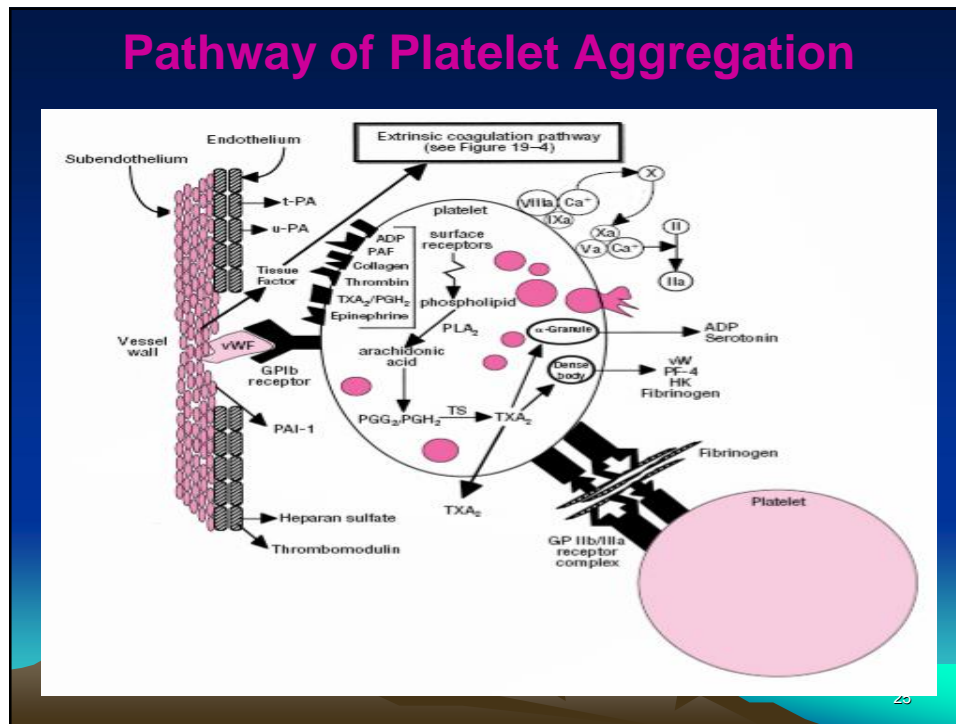
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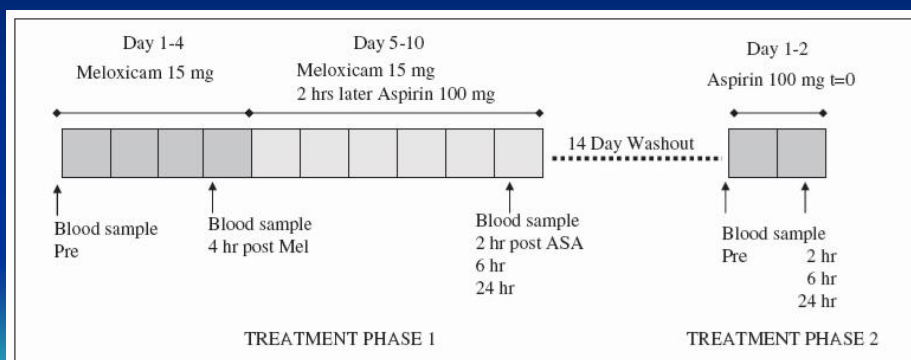
Intepretation of Maximum Aggregation Value (%)

Inductor	Hipo Agregasi Tendency	Normo Agregasi	Hiper Agregasi Tendency
Epinefrin	1-34	35-70	$\geq 71$
ADP	1-43	43-71	$\geq 72$
Kolagen	1-44	45-72	$\geq 73$
Slop	1-14	15-27	$\geq 28$

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- Similar study has been done (Ryn JV, 2004), but the design raises several questions ?



Ryn JV, 2004

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