Scientific literature suggests that maintaining a healthy lifestyle is effective in Preventing and controlling chronic diseases. It is well known that unhealthy diets, obesity, smoking and lack of physical exercise contribute to disease.

Scientific studies report lifestyle and nutrition have a significant effect in regulating the enzymatic action of cyclooxygenase-1&2 on arachidonic acid and the generation of thromboxane A2.

Levels of urinary 11-dehydrothromboxane B2 reflect activity of components of the thromboxane A2 pathway that result in thromboxane A2 generation.

Peer reviewed publications citing the thromboxane A2 pathway and urinary 11-dehydrothromboxane B2 (11-DHTXB2)

<table>
<thead>
<tr>
<th>Date</th>
<th>Journal</th>
<th>Report Type</th>
<th>Human/Animal</th>
<th>Subject #</th>
<th>11-DHTXB2 Test cited</th>
</tr>
</thead>
</table>
| 1.     | Cigarette smoking is associated with increased circulating proinflammatory and procoagulant markers in patients with chronic coronary artery disease: effects of aspirin treatment | 2005 • Am Heart J • Clinical Research • Human • 100 Subjects • 11-DHXTB2 | "After aspirin treatment, M-CSF, CRP, 11-dehydro-TXB 2, and prothrombin fragments 1+2 remained higher in smokers compared with nonsmokers despite a significant reduction of these markers by aspirin."
| 2.     | Effects of smoking cessation and nicotine substitution on systemic eicosanoid production in man | 2001 • Naunyn Schmiedebergs Arch Pharmacol • Clinical Research • Humans • 80 Subjects • 11-DHXTB2 | "The fact that eicosanoid production remains at pre-cessation level in volunteers who quit smoking but use nicotine substitution may be involved in the risk of cardiovascular complications reported during nicotine replacement therapy."
| 3.     | Cardiovascular biomarkers in groups of established smokers after a decade of smoking | 2009 • Basic Clin Pharmacol Toxicol • Clinical Research • Human • 11-DHXTB2 | "Significant statistical differences between smokers with approximately 10 years of smoking history and non-smokers in white cells count, hemoglobin and thromboxane turnover were seen, although they did not reach levels associated with overt diseases."
4. **Cyclooxygenase-1 mediated platelet reactivity in young male smokers**

2012 • Sage Journals • Clinical Research • Human • 25 Subjects • 11-DHTXB2

“Collagen-induced platelet aggregation and plasma/urinary thromboxane B<sub>2</sub> (TXB<sub>2</sub>) and 11-dehydroxythromboxane B<sub>2</sub> levels were higher in cigarette smokers compared to nonsmokers.”

“The levels of plasma/urinary TXB<sub>2</sub> were significantly increased an hour after cigarette smoking.”

5. **Platelet activation in obese women. Role of inflammation and oxidant stress**

2002 • JAMA • Clinical Research • Human • 93 Subjects • 11-DHTXB2

“Women with android obesity had higher levels of 8-iso PGF2alpha and 11-dehydro-TxB2 than nonobese women.”

“Both 8-iso PGF2alpha and 11-dehydroTxB2 were higher in women with android obesity than women with gynoid obesity”

“Of 20 women with android obesity, 11 achieved successful weight loss, which was associated with statistically significant reductions in C-reactive protein, 8-iso PGF2alpha and 11-dehydro-TXB2.

6. **Cross-sectional study of biomarkers of exposure and biological effect on monozygotic twins discordant for smoking**

2001 • Clin Chem Lab Med • Clinical Research • Human • 44 Subjects • 11-DHTXB2

“A subset of the BoBE, reported as being associated with inflammatory conditions and early stages of vascular disorders, has emerged as showing a consistent relationship with smoking status from the present and the previous studies.”

7. **Risk factors for carotid atherosclerosis and platelet activation**

1994 • Jpn Circ J • Clinical Research • Human • 24 Subjects • 11-DHTXB2

“Multivariate analysis indicated a significant positive correlation between urinary excretion of 11-dehydrothromboxane B2 and plaque score, age, smoking and hypercholesteremia.”

8. **Opposite effects of nicotinic acid and pyridoxine on systemic prostacyclin, thromboxane and leukotriene production in man**

2002 • Pharm Tox • Clinical Research • Human • 8 Subjects • 11-DHTXB2

“The treatment with nicotinic acid increased 11-DHTXB2 excretion to 2.6 fold and leukotriene E<sub>4</sub> excretion to twice the basal values.”
2010 • BMC Med Res Methodol • Clinical Research • Humans • 3585 Subjects • 11-DHTXB2

“Levels of WBC, EPI8, DEH11 and HDL were statistically associated with biomarkers of exposure to cigarette smoking and demographics and life style factors.”

10. A Japanese cross-sectional multicenter study of biomarkers associated with cardiovascular disease in smokers and non-smokers
2015 • Biomarkers • Clinical Research • Human • 670 smokers/356 non-smokers • 11-DHTXB2

“The mean hs-CRP concentration was not significantly different between the two groups of subjects.”

“We found that the 11-DTXB2 concentration was about 24% greater in smokers than in non-smokers, supporting the use of 11-DTXB2 as a potential biomarker for smoking and CVD.”
2015 • Res Devel • Clinical Research • Human • 731 Subjects • 11-DHTXB2

11. Nicotine effects on eicosanoid formation and hemostatic function: comparison of transdermal nicotine and cigarette smoking
1993 • JACC • Clinical Research • Human • 11-DHTXB2

“Cigarette smoking increased the urinary excretion of 11-dehydrothromboxane B2 (reflecting thromboxane A2 generation).”

“Cigarette smoking was also associated with higher levels of fibrinogen in plasma.”

“Cigarette smoking and transdermal nicotine treatment were both associated with a higher white blood cell count compared with the placebo patch.”

12. Olive oil and haemostasis: a review on its healthy effects
2006 • PHN • Clinical Review

“A diet enriched in virgin olive oil can reduce the sensitivity of platelets to aggregation, decreasing von Willebrand and thromboxane B2 plasma levels.

13. Suboptimal inhibition of platelet cyclooxygenase-1 by aspirin in metabolic syndrome
2012 • AHA • Clinical Research • Human • 181 Subjects • 11-DHTXB2

“Metabolic syndrome, which places patients at high risk for thrombotic cardiovascular events, strongly and uniquely associates with less effective inhibition of platelet COX-1 by aspirin.”
14. The effect of agility exercise on eicosanoid excretion, oxidant status, and plasma lactate in dogs
2012 • BMC Vet Res • Clinical Research • Dogs • 15 Subjects • 11-DHTXB2

“Alterations in the plasma post-exercise were likely due to hemoconcentration from insensible water loss, splenic contraction and sympathetic stimulation while 4-hours later autohemodilution reduced RBC parameters.”

15. Pentraxin 3 and platelet activation in obese patients after gastric banding
2015 • Jpn Cir J • Clinical Research • Human • 12 Subjects • 11-DHTXB2

“There is an association between inflammation, platelet activation and metabolic dysfunction in obesity, and PTX3 is a key player within these circuits.”

16. Endogenous secretory RAGE in obese women: association with platelet activation and oxidative stress
2012 • J Clin Endocrinol Metab • Clinical Research • Human • 100 Subjects • 11-DHTXB2

“Excess adiposity may be implicated in RAGE hyperactivation and thromboxane-dependent platelet activation, contributing to obesity-related metabolic and vascular disease.”

17. Impact of commonly prescribed exercise interventions on platelet activation in physically inactive and overweight men
2016 • Physiol Rep • Clinical Research • Human • 8 Subjects • 11-DHTXB2

18. Mediterranean diet reduces thromboxane A2 production in atrial fibrillation patients
2015 • Clin Nutr • Clinical Research • Human • 801 Subjects • 11-DHTXB2

“Med-Diet adherence is inversely associated to urinary excretion of 11-dehydro-TxB2, suggesting that Med-Diet may favorably affect platelet function in AF patients.”

19. Role of dietary polyphenols in the platelet aggregation network-a review of the in vitro studies
2006 • Nutraceutical Res • Clinical Review • Human • 11-DHTXB2

“The anti-aggregating effect depends in part on the specific structure of the phenol, even though great differences in anti-aggregating activity have been observed within each class.”

20. The cardiovascular effects of cocoa polyphenols-an overview
2016 • Diseases • Clinical Research • Humans • 11-DHTXB2

“Cocoa and cocoa polyphenols appear to exert promising cardioprotective effects in humans.”
21. **Effect of the flavonol quercetin on human platelet function: a review**

2015 • Food Pub Health • Clinical Review • Humans • 11-DHTXB2

“However, increasing evidence has indicated inadequate protection by antiplatelet therapy against thrombotic events in some patients.”

22. **The cardiovascular benefits of dark chocolate**

2015 • Vas Pharm • Clinical Review • 11-DHTXB2

“The effect of chocolate is more convoluted since the sucrose and lipid may transiently and negatively impact on endothelial function, partly through insulin signaling and nitric oxide bioavailability.”

23. **Natural sources of resveratrol and mechanisms of action with emphasis on cardiovascular disease: a brief review**

Clinical Review

“Epidemiological studies indicate that the consumption of red wine reduces the mortality and morbidity from CAD. Muscadine grapes contain high levels of antioxidants, including resveratrol, a polyphenol with multiple cardioprotective effects.”

24. **The role of polyphenols in causing cardiovascular disease**

2008 • Pharm • Clinical Review • Human • 11-DHTXB2

“The vascular endothelium is a critical regulator of vascular homeostasis, and endothelial dysfunction contributes to the pathogenesis and clinical expression of coronary artery disease.”

25. **Molecular targets of dietary polyphenols with anti-inflammatory properties**

2005 • Yonsei Med J • Clinical Review • Human

“Given that certain polyphenols are known to affect more than one protein, it is necessary consider possibility that any single compound may affect multiple mechanisms.”

26. **Effects of pomegranate juice and extract polyphenols on platelet function**

2009 • J Med Food • Clinical Review • Human

“We have shown that PJ reduces every step of platelet activation, such as platelet aggregation, calcium mobilization, hydrogen peroxide formation, and TxA2 production induced by collagen and arachidonic acid.”
27. Molecular targets of tea polyphenols in the cardiovascular system

2007 • Cardiovas Res • Clinical Review • Human

“By affecting the activity of receptor and signal transduction kinases, both catechins and theaflavins – the major ingredients of green and black tea, respectively – exert a variety of cardiovascular beneficial effects.”

Thromboxane A2 pathway schematics