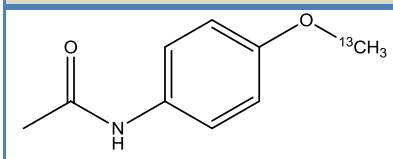
^{13}C-Methacetin Breath Test

^{13}C-Methacetin	
	Molecular weight: 166.19 g/mol Enrichment: 99 % Labeled C-atoms: 1 Dosage: 75 mg

Metabolism

Methacetin is metabolized rapidly in normal subjects, being highly extracted by the liver [1], implying that the metabolism of methacetin is mainly dependent on hepatic blood flow, the latter being generally decreased in cirrhotic patients [2]. Methacetin undergoes dealkylation by hepatic CYP1A2 to acetaminophen [3], with the methoxy group being eliminated as $^{13}CO_2$.

Published data of previous studies suggest that the Methacetin Breath Test is a rapid and precise quantitative liver function test without any evidence of toxicities related to the small doses used in contrast to other substrates [4–7].

Applications of ^{13}C-Methacetin Breath Test

The liver status of patients who have been diagnosed with liver disease can be assessed or monitored non-invasively using the ^{13}C-Methacetin Breath Test:

Condition	Assessment
Non-alcoholic steatohepatitis (NASH) or alcoholic steatohepatitis (ASH), Fibrosis or Cirrhosis	State of evolution (correlation with Child-Pugh Score) [8,9]
Fibrosis or Cirrhosis	State of evolution (correlation with Child-Pugh Score) [8,9]
Liver tumor	Hepatic reserve
Hepatitis B or C	Hepatic reserve [10]
Long-term medication e.g. anticonvulsants	Monitor hepatotoxicity
Liver transplant	Liver status of both donor and recipient[11,12]

Table 1: Liver diseases assessed by ^{13}C-Methacetin Breath Test

The patient should have fasted for 8 hours prior to the test. Smoking should also be avoided at least one hour prior to the test [13]. The patient should not drink carbonated water or soft drinks prior to the test since this might interfere with the results. In addition, oxygen supplementation should be avoided because increased oxygen content in exhaled breath can influence $^{13}CO_2$ measurement by NDIRS [14].

Test Performance Procedure (see IRIS® Operating Manual for additional information).

1. Collect zero (basal) breath sample as described in the manual.
2. Patient takes ^{13}C-Methacetin (75 mg) dissolved in water (100 ml).
3. Collect additional breath samples as shown below (Table 2).
4. Analyze all 10 breath samples with IRIS®-3 or IRIS®-Doc.

#1 Bag	#2 Bag	#3 Bag	#4 Bag	#5 Bag	#6 Bag	#7 Bag	#8 Bag	#9 Bag	#10 Bag
0 min	10 min	20 min	30 min	40 min	50 min	60 min	80 min	100 min	120 min

Table 2: ^{13}C-Methacetin Breath Test Sample Collection

Results and interpretation

In healthy subjects a peak in the exhaled Dose/h of labeled CO_2 is to be expected after 10 to 20 minutes (see Figure 1). About 30% of the administered dose is recovered as $^{13}CO_2$ after 120 minutes (see Figure 2). In general, the more severe the liver disease, the lower the % cum dose after 120 minutes.[8,10,15]

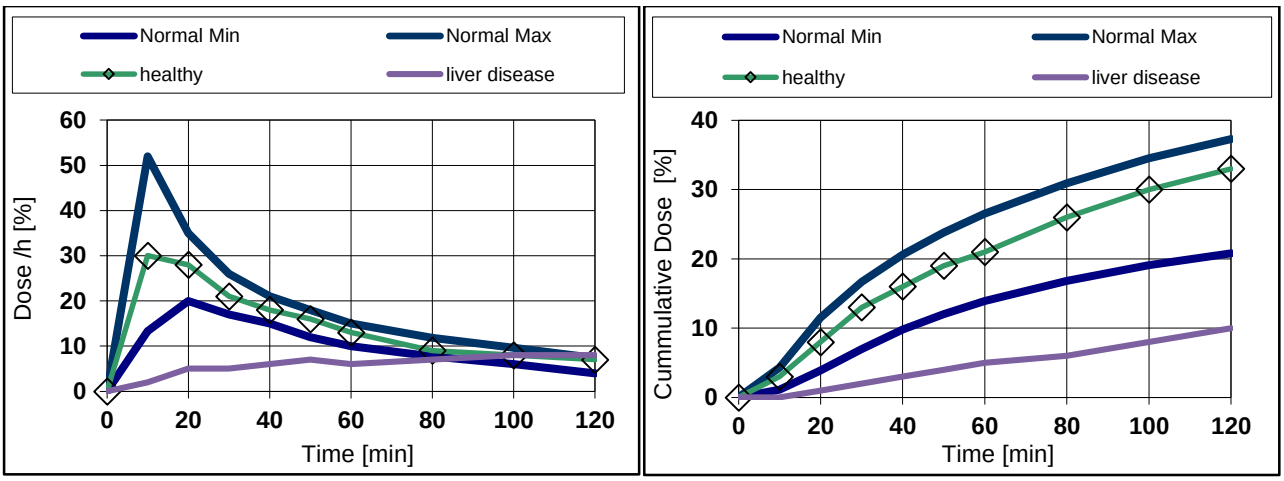


Fig. 1,2: ^{13}C-Methacetin Breath Test, Dose/h curve and % Cum Dose, healthy (normal) subject[16]

The value of the maximum metabolic rate (dose/h) has been shown to be a good quantitative predictor of cirrhosis and fibrosis in chronic hepatitis C (Table 3).

		Cut-off	Sensitivity	Specificity
Liver Cirrhosis	^{13}C-Methacetin Breath Test	< 14.6 %	92.6 %	84.1 %
	Fibroindex	> 1.82	70.4 %	91.3 %
Advanced Fibrosis	^{13}C-Methacetin Breath Test	< 21 ‰	75.4 %	79.5 %
	Fibroindex	> 1.35	66.7 %	84.6 %

Table 3: Comparison of ^{13}C-Methacetin Breath Test and FibroIndex as predictors of cirrhosis and fibrosis. (Adapted from Dinesen *et al*. [17])

The % cumulative dose at 120 minutes has been shown to correlate with different stages of liver disease (Table 4).

% Cumulative Dose, 120 min	Indication/ Correlation
31.0 (25.9 – 38.7)	Normal
13.6 (5.7 – 22.3)	Cirrhosis, Child-Pugh Class A
3.1 (1.1 – 16.5)	Cirrhosis, Child-Pugh Class B
0.6 (-1.1 – 3.5)	Cirrhosis, Child-Pugh Class C

Table 4: Correlation of ^{13}C-Methacetin Breath Test (% cum dose) with stage of liver disease [8]

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