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LIFECHANGINGMEDICINE

PSC and Your Liver: How to Keep Your Liver Healthy: Myths and Reality

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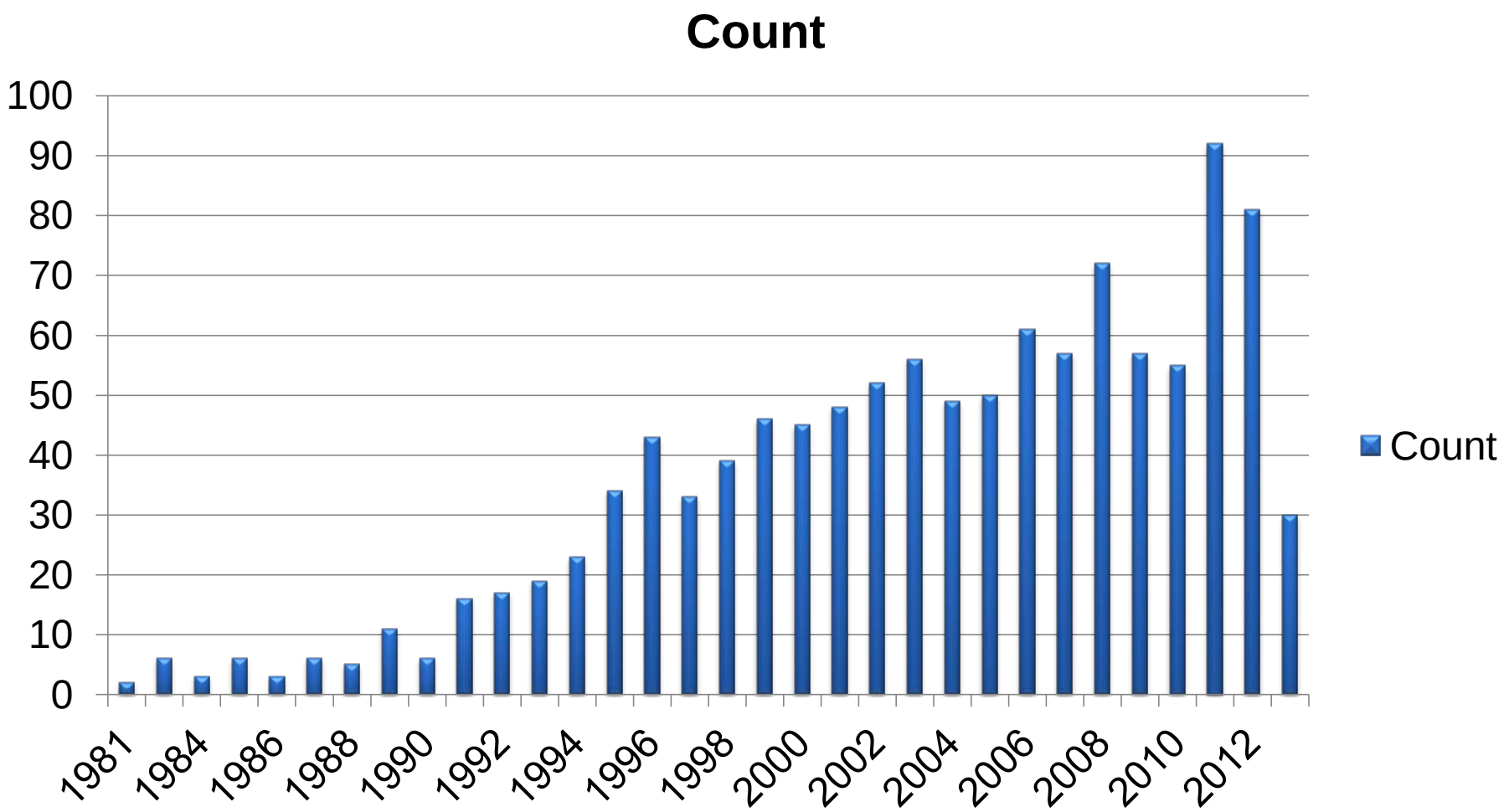
PSC Liver: Pubmed Publications



Overview

- Genetics and PSC: role of autoimmunity
- Alcohol and PSC
- Vitamin supplements in PSC
- Milk Thistle and Herbals
- Vancomycin and PSC
- Role of Coffee

Hot off the press: Dense genotyping of immune-related disease regions identifies nine new risk loci for primary sclerosing cholangitis

- The study was headed by Tom Karlsen and involved an international effort of investigators (including US, Canada, and Europe) and of course, PSC patients

- The findings have resulted in a better understanding of the genetic basis of PSC and how the genes of PSC overlap with the genes of several other autoimmune diseases

- The hope is that these findings can lead to new insights for targeting drugs that might already be in use for these more common diseases.

Nature Genetics ADVANCE ONLINE PUBLICATION
published online 21 April 2013; doi:10.1038/ng.2616

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PSC and Autoimmunity: The evidence

- The pathogenesis of PSC is poorly understood, and, owing to the lack of effective medical therapy, PSC remains a leading indicator for liver transplantation in northern Europe and the United States5, despite its relatively low prevalence (1 in 10,000)

- Affected individuals are diagnosed at a median age of 30–40 years and suffer from an increased frequency of IBD (60–80%)5,6 and autoimmune diseases (25%)

- Conversely, approximately only 5% of individuals with IBD develop PSC

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PSC and Autoimmunity: The evidence

- Sibling relative risk of 9- to 39-fold indicates a strong genetic component to PSC risk

- In addition to multiple strong associations within the HLA complex, recent association studies have identified genome-wide significant loci at 1p36 (MMEL1-TNFRSF14), 2q13 (BCL2L11), 2q37 (GPR35), 3p21 (MST1), 10p15 (IL2RA) and 18q21 (TCF4)

- Several theories have been proposed to explain the development of PSC5. The strong HLA associations and the clinical occurrence of PSC with immune-mediated diseases suggest that autoimmunity has a role in pathogenesis.

PSC and Autoimmunity: The evidence

- Seven immune-mediated diseases

- Crohn’s disease
- Celiac disease
- Psoriasis
- Rheumatoid arthritis
- Sarcoidosis
- Type 1 diabetes
- Ulcerative colitis

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PSC and Autoimmunity: The evidence

- The data convincingly show that genetic susceptibility to PSC extends considerably beyond risk factors involved in the closely related IBD phenotype and into autoimmune pathophysiology

- Furthermore, analysis of pleiotropic immune-related genetic variants highlights 33 additional suggestive loci in PSC, overall representing major new avenues for research into pathogenesis

Alcohol and PSC

- Little is known about risk factors for progression of fibrosis in primary sclerosing cholangitis (PSC) except for duration of disease and presence of symptoms

- Excessive consumption of alcohol causes liver diseas and a high intake of alcohol acts as a co-factor for progression of other chronic liver diseases, such as non-alcoholic steatohepatitis, hereditary hemochromatosis and hepatitis C (HCV)

World J Gastroenterol 2012 June 28; 18(24): 3105-3111

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Alcohol and PSC

- Heavy episodic drinking has been shown to be associated with progression of fibrosis in non-alcoholic fatty liver disease, alcohol consumption of more than 60 g per day increases the risk for cirrhosis 9-fold in patients with hereditary hemochromatosis, and an alcohol intake of more than 210 g per week in patients with HCV has been shown to increase fibrosis.

- The threshold for a safe intake of alcohol with regard to development of fibrosis in patients with concomitant liver disease is unclear and most patients with a chronic liver disease are advised to keep their alcohol intake to a minimum

Alcohol and PSC

- The impact of alcohol on progression of fibrosis in PSC has not been previously studied, although alcohol consumption has been reported to be associated with development of cholangiocarcinoma

- One of the most common questions from patients with PSC is: what amount of alcohol can be considered to be a safe intake?

Alcohol and PSC

- Patients with PSC have low alcohol consumption
- Only 9% consumed an amount of alcohol equal to or more than one unit per day
- There was a trend towards increased alcohol consumption after the PSC diagnosis in patients without significant fibrosis

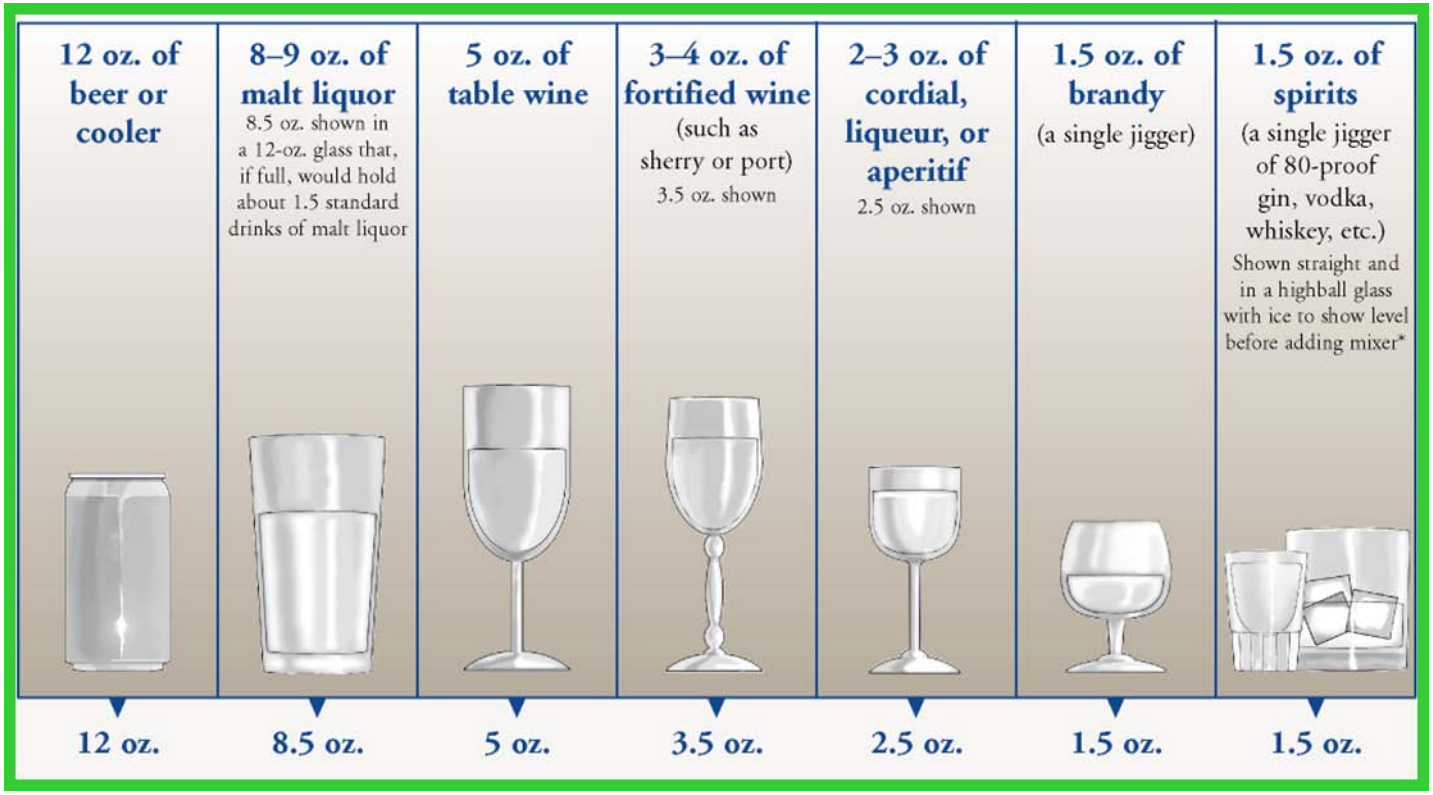
Alcohol and PSC

- No correlation between alcohol consumption and significant fibrosis

- In summary, these results indicate that low alcohol consumption is safe in patients with PSC

What is a Standard Drink?

In the U.S., a standard drink is any drink that contains about 14 grams of pure alcohol (about 0.6 fluid ounces or 1.2 tablespoons)



PSC: *Chronic Cholestasis*

- Pruritus
- Fat-soluble vitamin deficiency
- Metabolic Bone Disease
- Hyperlipidemia
- Steatorrhea

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PSC: *Fat-soluble Vitamin Deficiency*

- Vitamins A, D, E, K
- *Common – as patient progresses toward liver transplantation*

- Vitamin A deficiency: 40 %
- Vitamin D deficiency: 14 %
- Vitamin E deficiency: 2 %

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PSC: *Fat-soluble Vitamin Deficiency* Replacement Therapy

• Vitamin A	• 25-50,000 units 2-3 times per week
• Vitamin D	• 25-50,000 units 2-3 times per week
• Vitamin E	• 100 units twice daily
• Vitamin K	• 5 mg daily

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PSC: Preventive Medicine

- Hepatitis A vaccination
- Hepatitis B vaccination
- Influenza vaccination
- Pneumococcal vaccination

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PSC and Colorectal Cancer (CRC)

- Increased risk of CRC in patients with ulcerative colitis (UC) + PSC
- Risk increased by fourfold in patients with UC + PSC (UC alone)
- All PSC patients without a prior diagnosis of IBD – flexible sigmoidoscopy/random rectal biopsies
- PSC + UC: annual *colonoscopic surveillance*
- Incidence of CRC increased in patients with UC + PSC after liver transplantation

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Herbals and Liver Health

- From ongoing National Institute of Health clinical trials of herbal medicines provide more complete information on the risks and benefits from herbal medicine use in the general population

- Association with liver tumors
  - Ginkgo
  - Goldenseal
  - Kava

Herbals and Liver Health

- No evidence for carcinogenic activity
  - Ginseng
  - Milk Thistle
  - Turmeric oleoresin

Using Dietary Supplements Wisely

- Dietary supplements contain a variety of ingredients, such as vitamins, minerals, amino acids, and herbs or other botanicals. Research has confirmed health benefits of some dietary supplements but not others
- To use dietary supplements safely, read and follow the label instructions, and recognize that “natural” does not always mean “safe.” Be aware that an herbal supplement may contain dozens of compounds and that all of its ingredients may not be known
- Some dietary supplements may interact with medications or pose risks if you have medical problems or are going to have surgery. Most dietary supplements have not been tested in pregnant women, nursing mothers, or children

Using Dietary Supplements Wisely

- The U.S. Food and Drug Administration (FDA) regulates dietary supplements, but the regulations for dietary supplements are different and less strict than those for prescription or over-the-counter drugs

- Tell all your health care providers about any complementary health approaches you use. Give them a full picture of what you do to manage your health. This will help ensure coordinated and safe care

- Milk thistle is a flowering herb native to the Mediterranean region

- It has been used for thousands of years as a remedy for a variety of ailments, and historically was thought to have protective effects on the liver and improve its function

- Today, its primary folk uses include liver disorders such as cirrhosis and chronic hepatitis, and gallbladder disorders. Other folk uses include lowering cholesterol levels, reducing insulin resistance in people who have both type 2 diabetes and cirrhosis, and reducing the growth of breast, cervical, and prostate cancer cells

Milk Thistle: What the Science Says

- Previous laboratory studies suggested that milk thistle may benefit the liver by protecting and promoting the growth of liver cells, fighting oxidation (a chemical process that can damage cells), and inhibiting inflammation. However, results from small clinical trials of milk thistle for liver diseases have been mixed, and two rigorously designed studies found no benefit

- A 2012 clinical trial, cofunded by NCCAM and the National Institute of Diabetes and Digestive and Kidney Diseases, showed that two higher-than-usual doses of silymarin were no better than placebo for chronic hepatitis C in people who had not responded to standard antiviral treatment

Milk Thistle: What the Science Says

- The 2008 Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis (HALT-C) study, sponsored by the National Institutes of Health (NIH), found that hepatitis C patients who used silymarin had fewer and milder symptoms of liver disease and somewhat better quality of life but no change in virus activity or liver inflammation

Milk Thistle and Liver Disease

- Effect of silymarin (milk thistle) on liver disease in patients with chronic hepatitis C unsuccessfully treated with interferon therapy: a randomized controlled trial

- Higher than customary doses of silymarin did not significantly reduce serum ALT levels more than placebo in participants with chronic HCV infection unsuccessfully treated with interferon-based therapy

JAMA. 2012 Jul 18;308(3):274-82. doi: 10.1001/jama.2012.8265.

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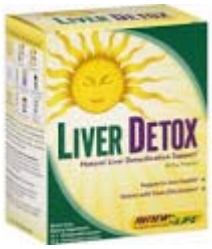
S-Adenosyl-L-Methionine (SAMe)

- Research has provided hints that SAMe might be helpful for depression, osteoarthritis, and a liver condition that can occur during pregnancy

- However, there is no conclusive evidence about whether SAMe is useful for these diseases

- SAMe may interact with medicines, and data on the long-term safety of SAMe and on its safety for use during pregnancy are too limited to make any conclusions

Liver Cleansers: Shop by brand



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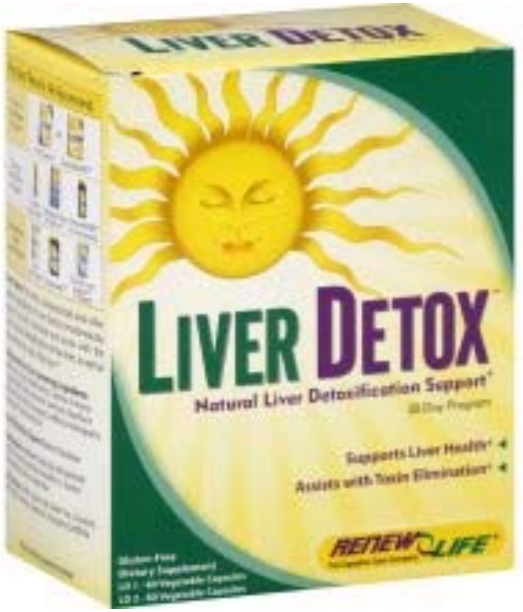
Liver Cleanse

- Dietary Supplement. Established 1981. Total body cleansing system. 2 of 8. A synergistic blend of herbs and vitamins for healthy liver function. A healthy liver is an essential part of maintaining optimum health. Liver Cleanse contains special ingredients designed to target irritants that affect the liver and production of bile and other digestive enzymes. (These statements have not been evaluated by the Food & Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.)

Liver Detox


LIVER DETOX
LIVER DETOX
Natural Liver Detoxification Support
RENEW LIFE

Liver Detox

- Dietary Supplement. Natural liver detoxification support. Liver Detox 1 (Morning Formula) - 60 vegetable capsules. Liver Detox 2 (Evening Formula) - 60 vegetable capsules. Supports liver health. Assists with toxin elimination. Gluten-free. Renew Life - the digestive care company. Contains no yeast, wheat, corn, gluten, salt, sugar, dairy, animal products, binders, fillers or artificial ingredients. Liver Detox:
- The herbs, nutraceuticals and other natural ingredients in Liver Detox simultaneously support, protect, stimulate and assist with the body's natural detoxification of the liver, as well as help protect the cells of the liver

Liver Detox

- Hepatoprotective (liver-protecting) ingredients: alpha lipoic acid, l-methionine, l-taurine, n-acetyl-cysteine, milk thistle, turmeric, selenium, boerhavia diffusa, eclipta alba, tinospora cordifolia, andrographis paniculata, picrorhiza kurroa. Bowel Elimination Support: belleric myrobalan. Cholagogues (ingredients that help stimulate bile flow in the liver): artichoke, dandelion, l-taurine, phosphatidylcholine, eclipta alba. Antioxidants: alpha lipoic acid, green tea, l-taurine, milk thistle, turmeric, selenium, tinospora cordifolia. This is a non-laxative formula.

Liver Detox

- For over a decade ReNew Life has been helping millions of people live healthier lives through better digestion and nutrition. Founded by best-selling author and PBS mainstay Brenda Watson after her own battle with poor health, it is now the leading cleansing and digestive care company in America. Brenda's passion and dedication have been instrumental in developing a complete line of premium herbal cleansing formulas and nutritional supplements for every need. Manufactured in a GMP and kosher facility. (This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.)

Vancomycin in PSC

- Oral Vancomycin is a viable treatment for early stage PSC, before extensive cirrhosis of the liver is present

- An extended clinical study demonstrated that long-term treatment with oral Vancomycin in fourteen juvenile PSC with IBD cases led to the normalization of liver blood markers and reversal of histological abnormalities

- However, relapse in GGT and ALT occurred after treatment was suspended

Vancomycin in PSC

- Oral Vancomycin is an immunomodulating bacteria glycopeptide antibiotic that is used to treat gram-positive infections with staphylococcal and has been shown to be poorly absorbed systemically

- Vancomycin could also be acting as an anti-inflammatory agent, suggesting that PSC could be an autoimmune disease

- The successful use of oral Vancomycin in reversing the effects of early stage PSC can help develop current understanding regarding the mechanism of the disease

Vancomycin in PSC

- Ongoing clinical trials can potentially lead to new information in regard to the etiology and pathology of the disease.

- Specifically, this case demonstrates that oral Vancomycin was effective in a case of recurrent PSC after OLT, suggesting that the disease mechanism is not confined within the liver and has external causes—potentially from the backflow of gut bacteria or the spread of gut bacteria through the blood.
- However, larger cohorts of children with PSC are needed for a more thorough, longitudinal investigation regarding the mechanism, pathogenesis, and treatment of juvenile PSC

Coffee and Liver Disease: Is It Time to Write a Prescription for Coffee?

- Coffee is ubiquitous in our society and has recently been shown to be inversely associated with total and cause-specific mortality

- Specific to the study of liver disease, coffee has been demonstrated to have beneficial effects on weight gain, development of diabetes, the prevention of hepatic fibrosis in NAFLD, and other chronic liver diseases, including chronic hepatitis C, as well as reduction of HCC

http://dx.doi.org/10.1053/j.gastro.2013.02.015

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Coffee and Liver Disease: Is It Time to Write a Prescription for Coffee?

- One large, retrospective survey of patients who participated in a NAFLD prevalence study found caffeinated coffee intake was associated with a significant reduction in fibrosis among biopsy-proven nonalcoholic steatohepatitis patients

- Similarly, a meta-analysis with pooled data from 457,922 participants demonstrated an inverse association between coffee and risk of incident diabetes

- Reduced hepatic fibrosis seems to be specific to caffeinated coffee and does not seem to be shared by other caffeinated beverages

Coffee and Liver Disease: Is It Time to Write a Prescription for Coffee?

- Based on the available data from predominantly observational trials, there seems to be a clinical benefit of coffee consumption for those patients at risk of developing hepatic fibrosis either from NAFLD or viral hepatitis

- Rates of liver cancer and the development of metabolic syndrome may also be improved with daily moderate filtered coffee intake

Coffee and Liver Disease: Is It Time to Write a Prescription for Coffee?

- It is unclear whether any of these benefits are significant enough to “treat” patients with chronic liver disease and further study is required with standard doses of each of these purported therapies in appropriately powered, multicenter, randomized, controlled trials with both biochemical and hepatic histology as endpoints

- In the interim, moderate daily unsweetened coffee ingestion is a reasonable adjunct to therapy for NAFLD patients that often includes lifestyle modification with diet and exercise

Thank You

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