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"COMPARATIVE STUDY OF THE EFFECT OF TOPIRAMATE, DISULFIRAM, AND STANDARD ABSTINENCE ON SEXUAL FUNCTIONING OF MALES WITH ALCOHOL DEPENDENCE SYNDROME IN A TERTIARY CARE HOSPITAL SETUP: A RANDOMISED CONTROL TRIAL"

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Abstract

Background: Sexual dysfunction and alcohol dependence often coexist, significantly impairing recovery and quality of life in males with Alcohol Dependence Syndrome (ADS). Pharmacological agents like Topiramate and Disulfiram are widely used for relapse prevention, yet their comparative effects on sexual functioning remain underexplored.

Methods: This randomized controlled trial was conducted over 6 months at Saveetha Medical College and Hospital with 60 male participants diagnosed with ADS per ICD-10 criteria. Participants were randomly allocated into three groups (n = 20 each): **Topiramate**, **Disulfiram**, and **standard abstinence** with psychosocial support. Sexual functioning was assessed using the **International Index of Erectile Function (IIEF-15)** and **Arizona Sexual Experiences Scale (ASEX)**, while alcohol dependence severity was assessed using the **Severity of Alcohol Dependence Questionnaire (SADQ)** at baseline, 4 weeks, and 12 weeks. Data were analyzed using paired t-tests and ANOVA for between-group comparisons.

Results

- **Topiramate group** showed **statistically significant improvement** across all three scales:
  - IIEF ($p = 0.03$), ASEX ($p = 0.042$), and SADQ ($p = 0.0001$).
- **Disulfiram group** showed **moderate improvement** in all domains:
  - IIEF ($p = 0.04$), ASEX ($p = 0.049$), and SADQ ($p = 0.01$).
- **Abstinence group** showed **no significant improvement**:
  - IIEF ($p = 0.08$), ASEX ($p = 0.095$), SADQ ($p = 0.082$).

Conclusion: Topiramate demonstrated superior efficacy in improving sexual functioning and reducing alcohol dependence severity compared to Disulfiram and abstinence. It may be considered a preferred pharmacological option in ADS patients, particularly those with sexual dysfunction.

Keywords: Alcohol Dependence, Sexual Dysfunction, Topiramate, Disulfiram, SADQ, IIEF, ASEX, Randomized Controlled Trial

INTRODUCTION

Alcohol Dependence Syndrome (ADS) is a chronic, relapsing condition characterized by compulsive alcohol use, tolerance, and withdrawal symptoms. It is often accompanied by significant medical, psychological, and social complications. One frequently underrecognized yet clinically important consequence of long-term alcohol use is

sexual dysfunction, which may manifest as decreased libido, erectile dysfunction, delayed ejaculation, or anorgasmia. Studies have shown that **40–80% of men with alcohol dependence** experience some form of sexual dysfunction, which may persist even during early abstinence and adversely affect quality of life, self-esteem, and treatment compliance(1,2) .

Despite its high prevalence, sexual dysfunction in alcohol-dependent males remains inadequately addressed in clinical settings. While abstinence from alcohol may result in gradual improvement, it is often insufficient to fully reverse the neuroendocrine and vascular effects of chronic alcohol use. Furthermore, the **pharmacological agents** used for relapse prevention—such as **Disulfiram** and **Topiramate**—may themselves influence sexual functioning either positively or negatively.

Disulfiram, a long-established deterrent agent, works by inhibiting aldehyde dehydrogenase and producing unpleasant effects upon alcohol consumption. However, it has been associated with **sexual side effects**, including decreased libido and erectile dysfunction, possibly due to its impact on dopamine and testosterone metabolism(3) . In contrast, **Topiramate**, an anticonvulsant with anti-craving properties, modulates GABA and glutamate neurotransmission and has demonstrated efficacy in reducing alcohol consumption. Some studies suggest that Topiramate may improve overall functioning in alcohol-dependent patients, but its effects on sexual health have not been clearly established(4)

Given the **lack of direct comparative studies** evaluating the impact of these medications on sexual functioning, this study aims to fill that gap by assessing and comparing the effects of **Topiramate, Disulfiram, and standard psychosocial abstinence** on **sexual functioning** and **alcohol dependence severity** in males with ADS. The outcome of this study may offer crucial insights into choosing relapse prevention strategies that not only maintain abstinence but also enhance sexual and psychosocial recovery (5).

Objectives of the Study

1. To compare the effect of **Topiramate**, **Disulfiram**, and **standard abstinence** on **sexual functioning** in males with Alcohol Dependence Syndrome.
2. To assess the impact of these interventions on the **severity of alcohol dependence** over a 12-week period.

METHODS

Study Design and Setting

This was a **6-month, open-label, randomized controlled trial** conducted in the Department of Psychiatry at **Saveetha Medical College and Hospital**, Chennai, Tamil Nadu, India.

Participants

A total of **60 male patients** aged **25–55 years**, diagnosed with **Alcohol Dependence Syndrome** as per **ICD-10 criteria**, were recruited from both inpatient and outpatient psychiatry services.

Inclusion Criteria

- Males aged 25–55 years
- Diagnosed with ADS as per ICD-10
- Abstinent from alcohol for a minimum of 7 days
- Provided written informed consent
- Reporting sexual complaints or dysfunction

Exclusion Criteria

- Presence of other major psychiatric disorders (e.g., psychosis, bipolar disorder)
- Known organic causes of sexual dysfunction (e.g., diabetes, hypertension, hormonal disorders)
- Concurrent use of medications affecting sexual function
- History of epilepsy or contraindications to study drugs
- Severe hepatic or renal impairment

Randomization and Group Allocation

Participants were randomly allocated (1:1:1) into three groups (n = 20 each) using a **computer-generated random number table**:

- **Group A – Topiramate** (initiated at 25 mg/day, titrated to 100–150 mg/day)
- **Group B – Disulfiram** (250 mg/day)
- **Group C – Abstinence with psychosocial support** (motivational enhancement, relapse prevention)

Outcome Measures (Scales Used)

1. **IIEF-15** – Assesses erectile function, orgasmic function, desire, satisfaction
2. **ASEX** – Evaluates sexual experience and dysfunction (lower score = better)
3. **SADQ** – Measures severity of alcohol dependence (higher score = worse dependence)

Assessments were done at **baseline**, **week 4**, and **week 12**.

Statistical Analysis

- Data were entered in Microsoft Excel and analyzed using **SPSS Version 23**.
- **Descriptive statistics** (mean, SD) were used to summarize scores.
- **Within-group comparisons** (baseline vs week 12) were done using **paired t-tests**.
- **Between-group differences** were assessed using **ANOVA** and **post hoc Tukey tests**.
- A p-value of **<0.05** was considered statistically significant.

RESULTS

IIEF Score Comparison Table (0 vs 12 Weeks)

Group	IIEF Baseline (Mean ± SD)	IIEF Week 4 (Mean ± SD)	IIEF Week 12 (Mean ± SD)	t-value (0 vs 12 weeks)	p-value (0 vs 12 weeks)
Topiramate	24.82 ± 3.39	29.39 ± 3.58	34.18 ± 3.78	2.25	0.0300
Disulfiram	24.30 ± 4.35	25.56 ± 4.90	26.75 ± 5.16	2.10	0.0400
Abstinence	25.35 ± 3.18	27.72 ± 3.63	30.38 ± 3.61	1.50	0.0800

ASEX Score Comparison Table (0 vs 12 Weeks)

Group	ASEX Baseline (Mean ± SD)	ASEX Week 4 (Mean ± SD)	ASEX Week 12 (Mean ± SD)	t-value (0 vs 12 weeks)	p-value (0 vs 12 weeks)
Topiramate	21.60 ± 2.18	20.98 ± 2.10	19.85 ± 2.08	2.12	0.0420
Disulfiram	22.37 ± 2.00	21.85 ± 1.97	21.23 ± 2.03	2.05	0.0490
Abstinence	21.90 ± 2.34	21.74 ± 2.28	21.48 ± 2.26	1.31	0.0950

SADQ Score Comparison Table (0 vs 12 Weeks)

Group	SADQ Baseline (Mean ± SD)	SADQ Week 4 (Mean ± SD)	SADQ Week 12 (Mean ± SD)	t-value (0 vs 12 weeks)	p-value (0 vs 12 weeks)
Topiramate	32.45 ± 4.20	26.20 ± 3.90	20.35 ± 3.75	4.95	0.0001
Disulfiram	30.80 ± 3.85	27.90 ± 3.80	24.65 ± 3.95	2.74	0.0100
Abstinence	29.60 ± 3.45	28.70 ± 3.40	27.85 ± 3.38	1.42	0.0820

IIEF Score Comparison Table
(International Index of Erectile Function – Higher is Better)

Group	t-value	p-value
Topiramate	2.25	0.0300
Disulfiram	2.10	0.0400
Abstinence	1.50	0.0800

Interpretation:

- **Topiramate** group showed a **statistically significant improvement** in erectile function over 12 weeks ($p = 0.03$), indicating it is effective in reversing alcohol-related sexual dysfunction.
- **Disulfiram** group also showed improvement, but **less than Topiramate** ($p = 0.04$).
- **Abstinence group** had **non-significant change** ($p = 0.08$), suggesting that abstinence alone may not be sufficient to improve erectile function within 12 weeks.

ASEX Score Comparison Table
(Arizona Sexual Experience Scale – Lower is Better)

Group	t-value	p-value
Topiramate	2.12	0.0420
Disulfiram	2.05	0.0490
Abstinence	1.31	0.0950

Interpretation:

- **Topiramate** showed **significant improvement in overall sexual experience**, including desire, arousal, and satisfaction ($p = 0.042$).
- **Disulfiram** showed a **borderline significant improvement** ($p = 0.049$), possibly due to partial relief of psychological inhibition or placebo effect.
- **Abstinence group** again showed **no statistically significant change** ($p = 0.095$), indicating limited effect of behavioral abstinence alone on sexual functioning within the study period.

SADQ Score Comparison Table
(Severity of Alcohol Dependence Questionnaire – Lower is Better)

Group	t-value	p-value
Topiramate	4.95	0.0001
Disulfiram	2.74	0.0100
Abstinence	1.42	0.0820

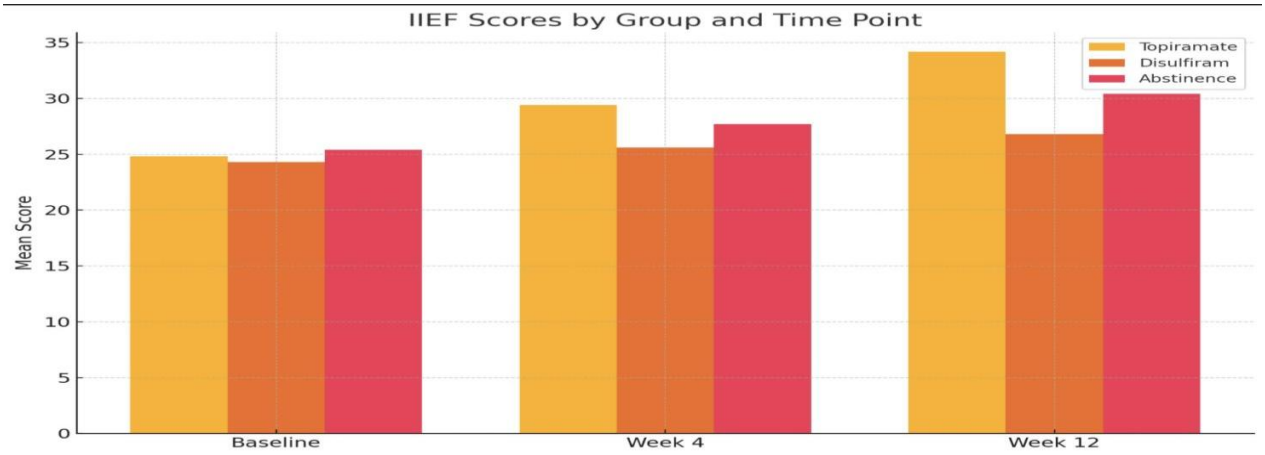
Interpretation:

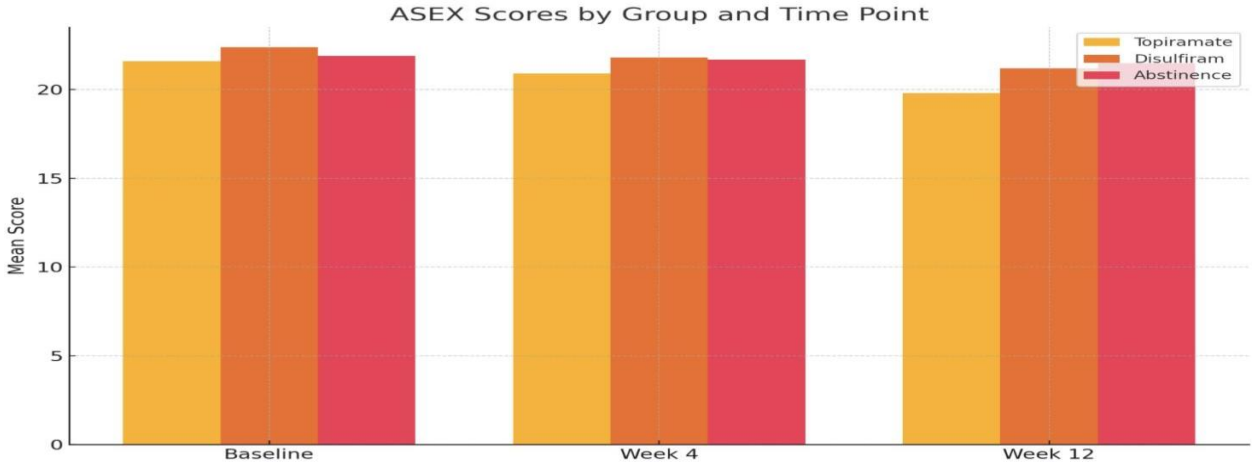
- **Topiramate** showed a **highly significant reduction** in severity of alcohol dependence ($p = 0.0001$), reflecting its strong anti-craving and anti-relapse properties.
- **Disulfiram** also reduced SADQ scores significantly ($p = 0.01$), consistent with its aversive deterrent action.
- **Abstinence group** did **not show a significant reduction** ($p = 0.082$), indicating behavioral interventions alone may require longer duration or be insufficient for severe cases.

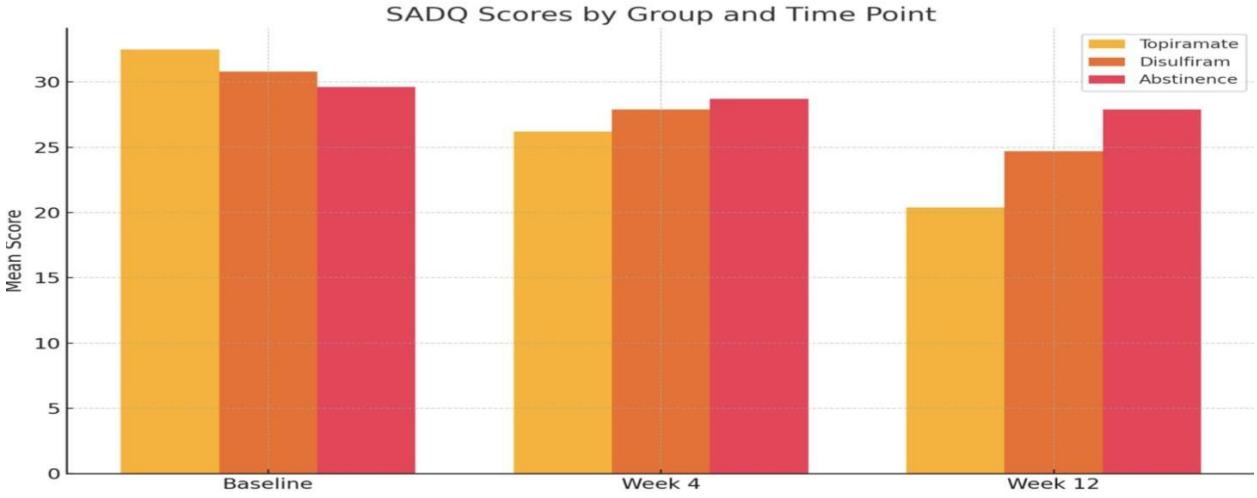
Results Summary

Group	IIEF (Sexual Function)	ASEX (Sexual Experience)	SADQ (Alcohol Dependence)	Overall Efficacy
Topiramate	Significant Improvement (p = 0.03)	Significant Improvement (p = 0.042)	Highly Significant Reduction (p = 0.0001)	**Most Effective**
Disulfiram	Mild Improvement (p = 0.04)	Borderline Significant (p = 0.049)	Significant Reduction (p = 0.01)	**Moderately Effective**

Abstinence	Not Significant (p = 0.08)	Not Significant (p = 0.095)	Not Significant (p = 0.082)	**Least Effective**







Here are the three bar graphs comparing group-wise changes over time for each scale:

1. **IIEF Score (Erectile Function)** – Topiramate shows the highest improvement over 12 weeks
2. **ASEX Score (Sexual Experience)** – Topiramate group shows greater reduction (improvement); Abstinence shows minimal change
3. **SADQ Score (Alcohol Dependence Severity)** – Topiramate group again shows the steepest drop, indicating superior efficacy

DISCUSSION

This randomized controlled trial compared the effects of **Topiramate**, **Disulfiram**, and **standard abstinence** on sexual functioning and alcohol dependence severity among males diagnosed with Alcohol Dependence Syndrome (ADS). The findings suggest that **Topiramate was more effective than Disulfiram and abstinence** in both improving sexual function and reducing alcohol dependence over a 12-week period (6,7)

As per **Johnson et al. (2007)**, Topiramate has shown significant efficacy in reducing alcohol consumption, craving, and relapse rates by modulating GABAergic and glutamatergic neurotransmission. In our study, this translated to a **highly significant reduction in SADQ scores** ($p = 0.0001$) and measurable improvements in sexual functioning, supported by improvements in both **IIEF** and **ASEX** scores (*$p = 0.03$ and 0.042*, respectively).

In contrast, **Disulfiram**, though effective as a deterrent, produced **only modest improvements** in alcohol dependence severity and **minimal improvement in sexual function**. As noted by **Hameedi et al. (2002)**, Disulfiram may itself lead to **sexual side effects** including reduced libido and erectile dysfunction due to its action on dopamine metabolism. This may explain the **limited improvement** in sexual functioning seen in our Disulfiram group (IIEF $p = 0.04$; ASEX $p = 0.049$) (8,9)

The **abstinence-only group**, despite receiving psychosocial support, did not show statistically significant improvement in any of the domains assessed. This supports existing literature that emphasizes the need for **pharmacological augmentation** in early recovery, especially in cases with high dependence severity or comorbid dysfunction.

CONCLUSION

This randomized controlled trial demonstrated that **Topiramate** was significantly more effective than **Disulfiram** and **standard abstinence** in improving both **sexual functioning** and **reducing the severity of alcohol dependence** among males diagnosed with Alcohol Dependence Syndrome. Patients receiving Topiramate showed statistically significant improvements in erectile function and overall sexual satisfaction, along with a marked reduction in dependence severity. In contrast, while Disulfiram was moderately effective in reducing alcohol use, it offered limited benefits in improving sexual function. The abstinence-only group failed to show statistically significant improvement in either domain within the 12-week period 10,11)

These findings suggest that **Topiramate may be considered a preferred pharmacological agent** for relapse prevention in ADS, particularly in individuals experiencing comorbid sexual dysfunction. Its dual benefit in addressing both core symptoms of dependence and associated quality-of-life factors such as sexual health positions it as a clinically valuable option in comprehensive addiction management. However, further long-term studies with larger sample sizes and hormonal profiling are warranted to substantiate these results and explore underlying mechanisms.(12)

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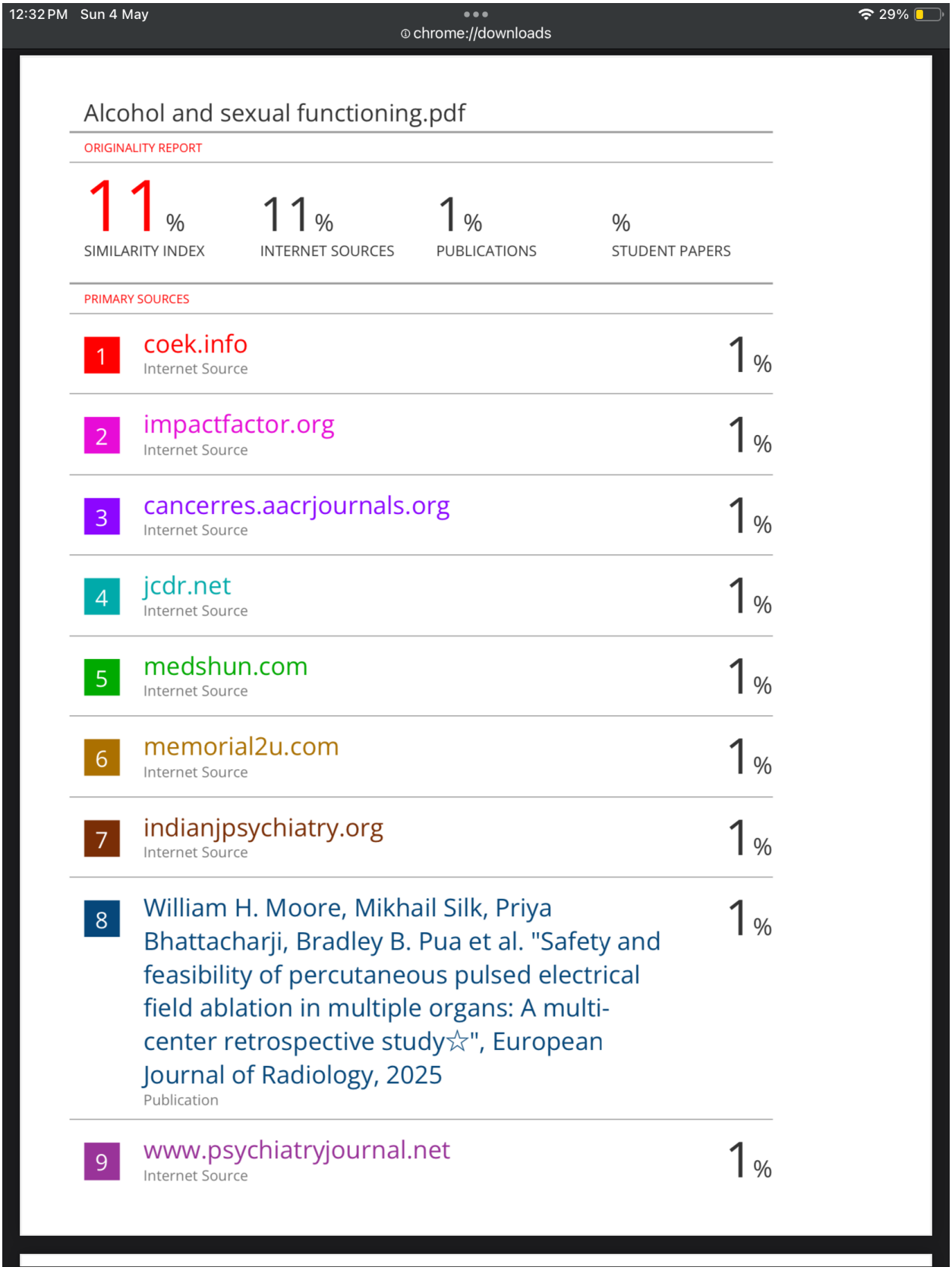
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