Urinary tyrosine detection for cancer screening and metabolic disorder diagnosis: a comprehensive evaluation of a colorimetric method

Filemon Silvano[1], Luiz Henrique Alvares dos Santos[1],
Carlos Eduardo Pires de Campos[2]

[1]Alunos de Graduação em Biomedicina Unisanta
[2]Biomédico Professor orientador Unisanta

Abstract:

Abnormal tyrosine metabolism has been observed in various malignancies and metabolic disorders. Urinary tyrosine detection represents a potential non-invasive approach for disease screening. This study aims to evaluate the clinical performance, analytical validity, and practical applications of a colorimetric urinary tyrosine detection method based on modified Millon's reagent for cancer screening and metabolic disorder diagnosis. A comprehensive analysis of clinical trial data involving 8,078 participants was conducted, including 4,375 cancer patients and 3,703 non-cancer controls. The colorimetric test was evaluated for sensitivity, specificity, and compared with high-performance liquid chromatography (HPLC) and spectrophotometry methods. Interference factors including dietary components and medications were systematically assessed. The colorimetric method demonstrated sensitivity of 96.69% and specificity of 99.40% for malignant tumor detection. Positive detection rates varied significantly across disease categories: malignant tumors (96.69%), pigmentary disorders (22.06%), diabetes (21.51%), and healthy individuals (0.60%). Comparison with HPLC showed maximum deviation of 11.4% in low-concentration ranges, with 0% deviation in high-concentration ranges (>500 mg/L). Dietary interference, particularly from seafood (23.3%), meats (20.0%), and alcohol/caffeine (16.7%), resolved completely within 48 hours of abstinence. The evaluated urinary tyrosine detection method shows high sensitivity and specificity for malignant tumor detection in this study population. The semi-quantitative colorimetric approach presents both advantages and limitations that warrant consideration for clinical implementation. Positive results require confirmatory diagnostic procedures.

Keywords: Urinary tyrosine, cancer screening, colorimetric assay, Millon's reagent, metabolic disorders, early detection

Detecção de Tirosina Urinária para Rastreamento de Câncer e Diagnóstico de Desordens Metabólicas: Uma Avaliação Abrangente de um Método Colorimétrico

Resumo:

Um metabolismo anormal da tirosina tem sido observado em várias neoplasias malignas e distúrbios metabólicos. A detecção de tirosina na urina representa uma abordagem potencial não invasiva para triagem de doenças. Este estudo tem como objetivo avaliar o desempenho clínico, a validade analítica e as aplicações práticas de um método colorimétrico de detecção de tirosina urinária baseado no reagente de Millon modificado, para triagem de câncer e diagnóstico de distúrbios metabólicos. Foi realizada uma análise abrangente de dados de ensaios clínicos envolvendo 8.078 participantes, incluindo 4.375 pacientes com câncer e 3.703 controles sem câncer. O teste colorimétrico foi avaliado quanto à sensibilidade, especificidade e comparado com métodos de cromatografia líquida de alta eficiência (HPLC) e espectrofotometria. Fatores de interferência, incluindo componentes alimentares e medicamentos, foram sistematicamente avaliados. O método colorimétrico demonstrou sensibilidade de 96,69% e especificidade de 99,40% para detecção de tumores malignos. As taxas de detecção positiva variaram

significativamente entre as categorias de doenças: tumores malignos (96,69%), distúrbios pigmentares (22,06%), diabetes (21,51%) e indivíduos saudáveis (0,60%). A comparação com HPLC mostrou desvio máximo de 11,4% em faixas de baixa concentração, com 0% de desvio em faixas de alta concentração (>500 mg/L). A interferência alimentar, especialmente de frutos do mar (23,3%), carnes (20,0%) e álcool/cafeína (16,7%), foi completamente resolvida após 48 horas de abstinência. O método avaliado de detecção de tirosina urinária apresenta alta sensibilidade e especificidade para detecção de tumores malignos nesta população estudada. A abordagem colorimétrica semiquantitativa apresenta vantagens e limitações que merecem consideração para implementação clínica. Resultados positivos requerem procedimentos diagnósticos confirmatórios.

Palavras-chave: Tirosina urinária, triagem de câncer, ensaio colorimétrico, reagente de Millon, distúrbios metabólicos, detecção precoce.

INTRODUCTION

Cancer remains a leading cause of mortality worldwide, with early detection significantly improving patient outcomes and survival rates (SUNG *et al.*, 2021, p. 210). Traditional cancer screening methods, while effective, often involve invasive procedures, substantial costs, or limited accessibility in certain healthcare settings (SMITH *et al.*, 2019, p. 185; CROSBY *et al.*, 2022, p. 1). The identification of non-invasive biomarkers that can indicate early metabolic changes associated with malignancy continues to be investigated in oncology diagnostics (COHEN *et al.*, 2018, p. 927).

Tyrosine, an aromatic amino acid, plays essential roles in protein synthesis and serves as a precursor for neurotransmitters including dopamine, norepinephrine, and epinephrine (FERNSTROM; FERNSTROM, 2007, p. 1541S; HOLEČEK, 2018, p. 33). Abnormal tyrosine metabolism has been documented in various pathological conditions, including malignant tumors, metabolic disorders, and neurodegenerative diseases (VUČKOVIĆ *et al.*, 2018, p. 480; WANG *et al.*, 2011, p. 450). Previous studies have reported that urinary tyrosine levels may increase in patients with malignant tumors, suggesting altered cellular metabolism (CASCINO *et al.*, 1995, p. 508; LAI *et al.*, 2005, p. 270).

The detection of monohydroxyphenol metabolites, particularly tyrosine, in urine has been proposed as a screening modality due to non-invasiveness and ease of sample collection (RAAB et al., 2006, p. 588). Classical methods for tyrosine quantification include high-performance liquid chromatography (HPLC), mass spectrometry, and enzymatic assays (PRINSEN et al., 2016, p. 655; LE et al., 2014, p. 170). However, these techniques often require sophisticated equipment and trained personnel (SUWANNARAT et al., 2005, p. 722).

Colorimetric methods based on Millon's reagent have been historically used for protein and phenolic compound detection (MILLON, 1849, p. 41; AITKEN; LEARMONTH, 2009, p. 4). The adaptation of this classical method for clinical diagnostics has been proposed for urinary tyrosine measurement. However, comprehensive evaluation of such colorimetric approaches remains limited in the literature. Critical questions persist regarding diagnostic performance across different cancer types, specificity in distinguishing malignant from benign conditions, interference from dietary and pharmaceutical sources, and correlation with established quantitative methods (PAVLOVA; THOMPSON, 2016, p. 30;

DEBERARDINIS; CHANDEL, 2016, p. 2).

This study presents a comprehensive evaluation of a colorimetric urinary tyrosine detection method, analyzing data from clinical trials involving over 8,000 participants. We assess the method's sensitivity and specificity across various disease categories, validate its performance against HPLC and spectrophotometry, characterize interference factors, and evaluate its potential clinical utility.

2. METHODS

This evaluation analyzed data from multiple clinical trials conducted across healthcare facilities in China. The study included 8,078 participants aged 18-60 years, comprising three primary groups: (1) cancer patients with histologically confirmed malignancies (n=4,375), (2) patients with non-malignant conditions including metabolic disorders and infectious diseases (n=1,041), and (3) healthy individuals serving as controls (n=2,662).

Cancer patients represented diverse malignancy types: gastrointestinal cancers (gastric, colorectal, liver), nasopharyngeal carcinoma, malignant lymphoma, breast cancer, gynecological malignancies, and lung cancer. Non-cancer patients included individuals diagnosed with pigmentary disorders, diabetes mellitus, gastritis, gastric ulcer, tuberculosis, viral hepatitis, benign prostatic hyperplasia, cholecystitis, and pneumonia. Healthy controls were recruited from individuals undergoing routine health examinations with no known medical conditions.

Exclusion criteria included: pregnancy, chronic renal disease, individuals on dialysis, patients with phenylketonuria or tyrosinemia, and those unable to provide informed consent. The study protocols received approval from institutional ethics committees, and all participants provided written informed consent.

2.1 PRINCIPLE OF DETECTION

The evaluated test employs a modified Millon's reagent method for detecting monohydroxyphenol metabolites, primarily tyrosine, in urine. The reagent contains mercury nitrate in nitric acid, which reacts with the phenolic hydroxyl group of tyrosine to form a colored complex. The intensity and hue of the color change correlate with tyrosine concentration, enabling semi-quantitative assessment.

Sample Collection: First-morning midstream urine samples (3 mL) were collected in sterile containers. Participants were instructed to avoid high-protein foods, dairy products, seafood, alcohol, and caffeine for 48 hours prior to testing.

Test Execution: The urine sample (3 mL) was added to an ampoule containing the reagent. The mixture was allowed to react at room temperature for 3-5 minutes.

Result Interpretation: The color change was compared to a standardized 8-color scale (Results No. 1-8), corresponding to tyrosine concentrations from 0 to 2000 mg/L. Results were categorized as:

- **Negative** (No. 1-3): Normal tyrosine concentration (0-200 mg/L)
- **Positive** (No. 4-5): Elevated tyrosine (250-324 mg/L)
- **High Positive** (No. 6-8): Significantly elevated tyrosine (≥500 mg/L)

2.2 HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC)

A subset of 875 cancer patient samples was analyzed using both the

colorimetric method and HPLC to assess correlation and deviation. The HPLC system (Vasian-5060) was equipped with a UV-100 ultraviolet detector operating at 280 nm. The mobile phase consisted of 15 mM phosphate buffer (pH 6.5) with a flow rate of 1.0 mL/min at 30°C column temperature. Urine samples required no pretreatment, and 10 μL injection volumes were used.

2.3 VISIBLE SPECTROPHOTOMETRY

An independent validation study involving 773 participants (620 healthy individuals and 153 cancer patients) employed visible spectrophotometry at 500 nm wavelength. The method utilized optimized reagent concentrations: 0.3 mL of 2 mol/L mercury nitrate, 0.5 mL of 0.01 mol/L $NaNO_2$, and 0.2 mL of 9 mol/L HNO_3 in a 3 mL reaction system. Optimal color development time was 36 minutes. Tyrosine showed linear response in the concentration range of 0.4-3.2 mmol/L.

2.4 DIETARY INTERFERENCE STUDY

A controlled study involving 210 healthy participants evaluated dietary interference effects. Subjects were divided into seven groups (n=30 each) and consumed specific food categories: (1) dairy products, (2) alcoholic and caffeinated beverages, (3) fruits (citrus, pineapple, banana, figs), (4) meats (liver, beef, sausage), (5) vegetables (tomatoes, beans, lentils), (6) seafood (sardines, tuna, oysters), and (7) pigment-rich foods (beets, dragon fruit). Testing was performed immediately after consumption and repeated 48 hours later.

2.5 MEDICATION INTERFERENCE ANALYSIS

Systematic review of pharmaceutical interference identified medications potentially affecting test results, including drugs causing false-positive results (hormonal drugs, amino acid supplements, traditional medicines, central nervous system drugs) and false-negative results (tyrosine inhibitors, salicylic acid derivatives, sedatives, analgesics, antihypertensive agents).

2.6 STATISTICAL ANALYSIS

Sensitivity was calculated as true positives (true positives + false negatives). Specificity was calculated as true negatives (true negatives + false positives). Positive predictive value (PPV) and negative predictive value (NPV) were computed where applicable. Correlation between the colorimetric method and HPLC was assessed using Pearson correlation coefficient. Deviation rates were calculated as the percentage difference between methods. Statistical significance was set at $p<0.05$.

3. RESULTS

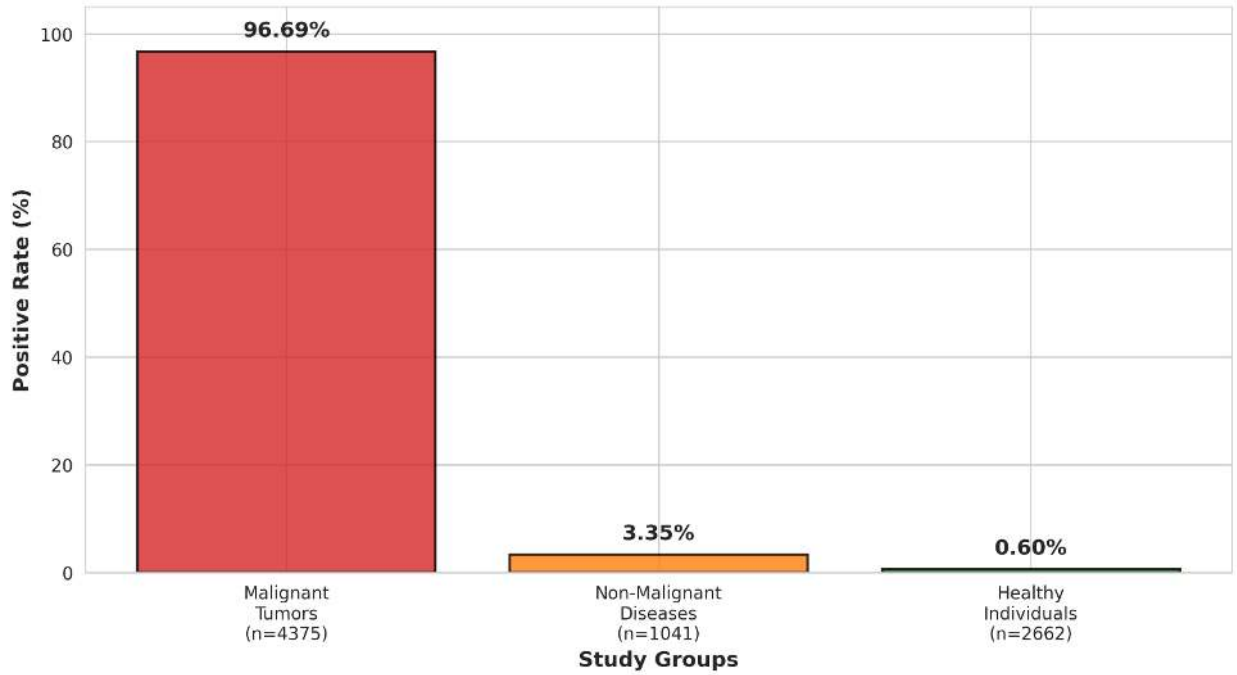
The colorimetric method demonstrated sensitivity of 96.69% (95% CI: 96.1-97.2%) for malignant tumor detection, with 4,230 of 4,375 cancer patients testing positive. In the healthy control group (n=2,662), 16 individuals tested positive, resulting in specificity of 99.40% (95% CI: 99.0-99.7%) (Table 1; Figure 2).

Table 1 – Clinical Trial Results Across Disease Categories

Disease Category	Sample Size (n)	Positive Cases	Negative Cases	Positive Rate (%)
Malignant Tumors	4375	4230	145	96.69
Pigmentary Disorders	68	15	53	22.06
Diabetes	93	20	73	21.51
Gastritis	166	25	141	15.06
Gastric Ulcer	78	11	67	14.10
Tuberculosis	56	5	51	8.93
Viral Hepatitis	102	9	93	8.82
Benign Prostatic Hyperplasia	28	2	26	7.14
Cholecystitis	115	8	107	6.96
Pneumonia	87	6	81	6.90
Healthy Individuals	2662	16	2646	0.60

Source: Adapted from Summary of clinical trials of CarciReagent tester kit in China.

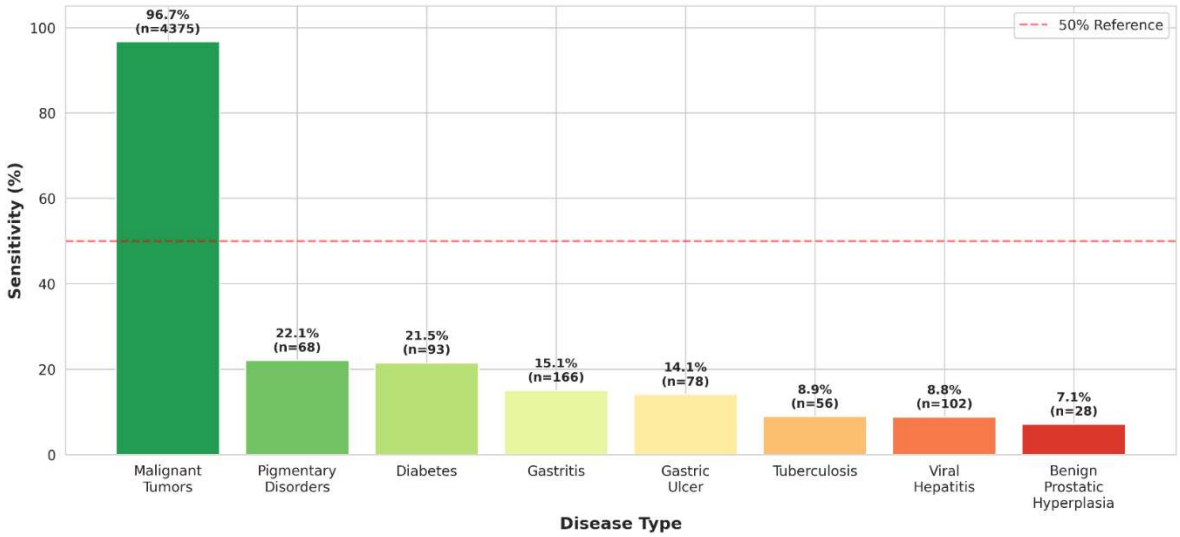
Figure 2 – Positive Detection Rates Across Study Groups



Source: Adapted from Summary of clinical trials of CarciReagent tester kit in China.

The positive detection rate varied significantly across disease categories ($p<0.001$). Malignant tumors showed the highest positive rate (96.69%), substantially exceeding non-malignant conditions: pigmentary disorders (22.06%), diabetes (21.51%), gastritis (15.06%), gastric ulcer (14.10%), tuberculosis (8.93%), viral hepatitis (8.82%), benign prostatic hyperplasia (7.14%), cholecystitis (6.96%), and pneumonia (6.90%) (Table 1; Figure 1).

Figure 1 – Sensitivity of CarciReagent Test Across Different Disease Types



Source: Adapted from Summary of clinical trials of CarciReagent tester kit in China.

Analysis of specific cancer types revealed variable positive rates (Table 5; Figure 1). Gynecological malignancies (ovarian and cervical cancer combined) demonstrated positive rate of 83.3% (n=70), with mean urinary tyrosine concentration of 940.9 mg/L (range: 873.6-1008.3 mg/L). Nasopharyngeal cancer showed 81.4% positivity (n=35) with mean tyrosine of 806.3 mg/L (range: 536.9-1073.8 mg/L). Gastric cancer exhibited 71.5% positivity (n=32) with mean tyrosine of 760.8 mg/L (range: 627.9-893.6 mg/L). Liver cancer demonstrated 70.0% positivity (n=31) with mean tyrosine of 562.4 mg/L (range: 364-760.8 mg/L).

Table 5 – Cancer Type-Specific Performance Metrics

Cancer Type	Sample Size	Positive Rate (%)	Mean Tyrosine (mg/L)	Range (mg/L)
Nasopharyngeal Cancer	35	81.4	806.3	536.9-1073.8
Ovarian/Cervical Cancer	70	83.3	940.9	873.6-1008.3
Liver Cancer	31	70.0	562.4	364-760.8
Gastric Cancer	32	71.5	760.8	627.9-893.6
Overall Malignant Tumors	4375	96.69	N/A	0-2000

Source: Adapted from Application of Visible Spectrophotometry Method to Detect Monohydroxyphenols in Urine.

The semi-quantitative nature of the test enabled categorization of tyrosine levels into clinically defined ranges (Table 3; Figure 3). Normal individuals predominantly exhibited results No. 1-3 (0-200 mg/L), corresponding to colorless, pale yellow, or reddish coloration. Cancer patients frequently demonstrated results No. 6-8 (≥500 mg/L), corresponding to brown-red to deep rust-red coloration.

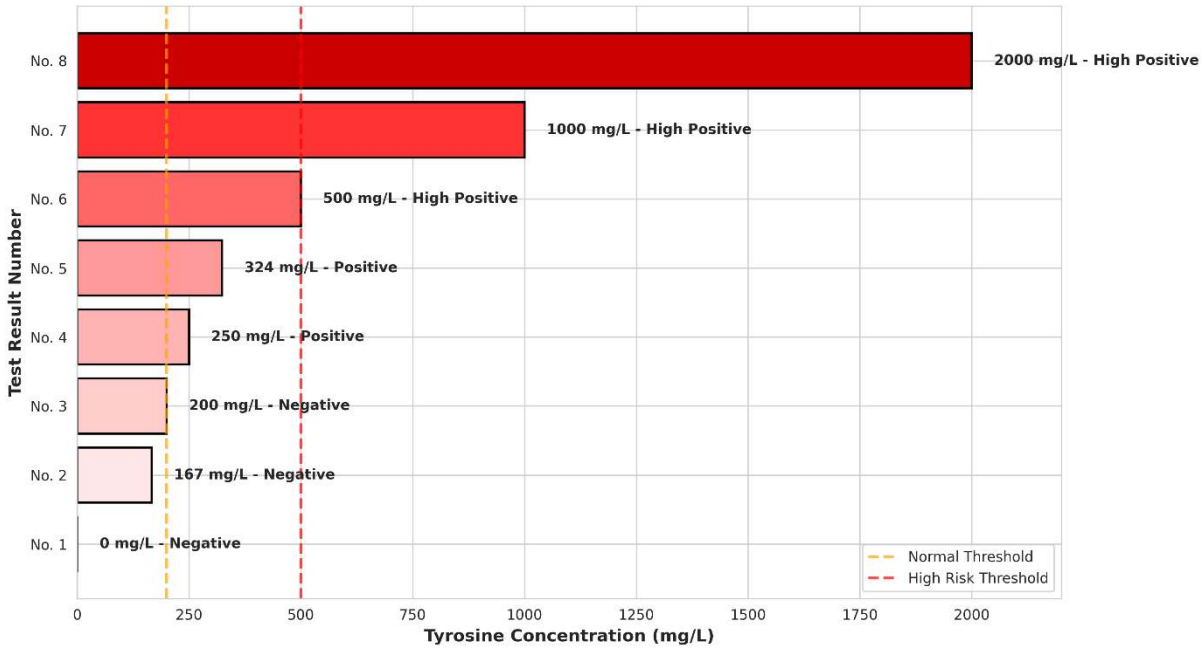
Table 3 – Tyrosine Concentration Ranges and Clinical Interpretation

Result Number	Concentration (mg/L)	Color Description	Clinical Interpretation
No.1	0	Colorless	Negative
No.2	167	Pale Yellow	Negative
No.3	200	Reddish	Negative
No.4	250	Light Red	Positive – Elevated
No.5	324	Pink/Rose Red	Positive – Elevated
No.6	500	Brown Red	High Positive – Serious Disease Risk
No.7	1000	Dark Rust Red	High Positive – Serious Disease Risk
No.8	2000	Deep Rust Red	High Positive – Serious Disease Risk

Source: Adapted from CarciReagent in Vitro diagnostic device user manual.

Among the 4,230 positive cancer cases, 68.4% (n=2,893) showed high positive results (≥500 mg/L), while 31.6% (n=1,337) showed moderately elevated results (250-499 mg/L).

Figure 3 – Tyrosine Concentration Ranges and Clinical Interpretation



Source: Adapted from CarciReagent in vitro diagnostic device user manual

Validation against HPLC in 875 cancer patient samples revealed concentration-dependent deviation patterns (Table 2; Figure 4). Maximum deviation of 11.4% occurred in the light red range (250±30 mg/L), where colorimetric readings showed overestimation compared to HPLC

values (195-237 mg/L). The pink range (333±60 mg/L) showed 7.7% deviation, while the rose red range (500±150 mg/L) exhibited 3.7% deviation.

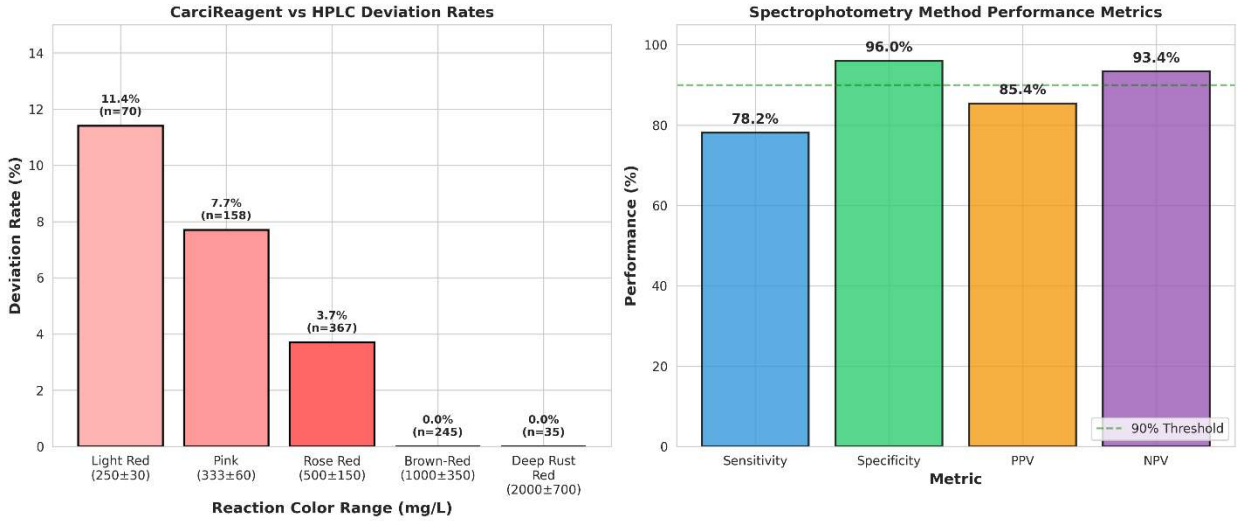
Table 2 – Performance Metric Comparison of Detection Methods

Method	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Sample Size
CarciReagent (Colorimetric)	96.69	99.40	N/A	N/A	8078
CarciReagent vs HPLC	Max deviation: 11.4	0 deviation (high range)	N/A	N/A	875
Spectrophotometry (500nm)	78.15	96.00	85.40	93.40	773

PPV: Positive Predictive Value; NPV: Negative Predictive Value; HPLC: High-Performance Liquid Chromatography

Source: Adapted from Summary of clinical trials; Comparison test of CarciReagent and HPLC method; Application of Visible Spectophotometry Method to detect monohydroxyphenols in Urine

Figure 4 – Colorimetric Method vs HPLC Deviation Rates and Spectrophotometry Performance Metrics



Source: Panel A adapted from Comparison test of CarciReagent and HPLC method; Panel B adapted from Applications of Visible Spectrophotometry Method to Detect Monohydroxyphenols in Urine

In the high-concentration ranges brown-red (1000±350 mg/L) and deep rust red (2000±700 mg/L) deviation rates were 0%, indicating concordance between methods. The overall correlation between the colorimetric method and HPLC was statistically significant ($r=0.94$, $p<0.001$).

The deviation in lower concentration ranges was attributed to natural urine color variation, specificity limitations of colorimetric detection, and potential interference from medications.

Independent validation using visible spectrophotometry at 500 nm wavelength in 773 participants provided additional performance metrics (Table 2). The spectrophotometric method achieved sensitivity of 78.15%, specificity of 96.00%, positive predictive value of 85.40%, and negative predictive value of 93.40%. Sample recovery experiments demonstrated average recovery of 98.1% with standard deviation of 1.9%.

Optical density (OD) values in cancer patient urine samples were significantly higher than healthy controls ($p<0.05$). Normal individuals showed OD of 0.11±0.089, corresponding to tyrosine content of 0.18-1.64 mmol/L (32.76-298.5 mg/L, median: 165.6 mg/L). Cancer patients demonstrated elevated OD values, with nasopharyngeal cancer at 0.54±0.18, gynecological cancers at 0.63±0.045, liver cancer at 0.37±0.14, and gastric cancer at 0.51±0.089.

3.1 DIETARY INTERFERENCE ASSESSMENT

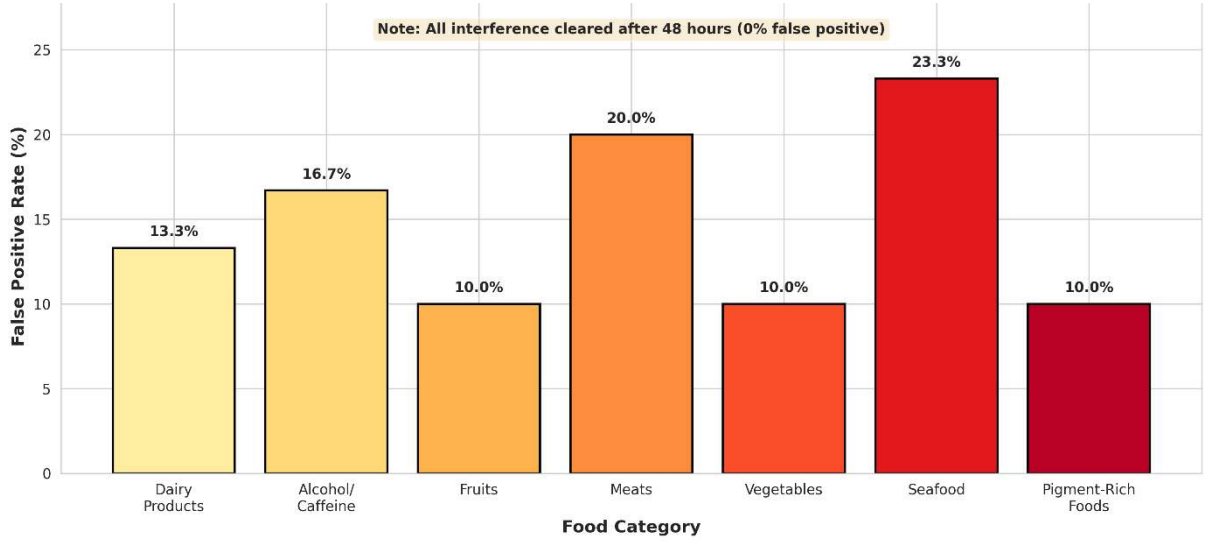
Systematic evaluation of dietary interference revealed transient effects (Table 4; Figure 5). Among 210 healthy participants consuming tyrosine-rich or pigment-rich foods, false-positive rates varied by food category: seafood (23.3%), meats (20.0%), alcohol/caffeine (16.7%), dairy products (13.3%), and fruits, vegetables, or pigment-rich foods (10.0% each).

Table 4 – Interference Factors and Recommendations

Interference Type	Effect	Recommendation
Hormonal Drugs	False Positive	Consult physician
Amino Acid Drugs	False Positive	Consult physician
Traditional Chinese Medicine	False Positive	Avoid 48h before test
Tyrosine Inhibitors	False Negative	Avoid 48h before test
Salicylic Acid Drugs	False Negative	Avoid 48h before test
Sedatives/Analgesics	False Negative	Consult physician
High-Protein Foods	False Positive	Avoid 48h before test
Dairy Products	False Positive (13.3%)	Avoid 48h before test
Seafood	False Positive (23.3%)	Avoid 48h before test
Alcohol/Caffeine	False Positive (16.7%)	Avoid 48h before test
Stress/Fatigue	False Positive	Adequate rest before test
Diabetes	False Negative	Not suitable for test
H.pylori Infection	False Negative	Not suitable for test

Source: Adapted from analysis of interference factors of CarciReagent test; Food interference test report

Figure 5 – Food Interference Factors on Test Results (Within 48 Hours)



Source: Adapted from Food Interference Factor Test Report

When the same participants were retested 48 hours after food consumption, all results returned to negative (0% false positive rate), demonstrating clearance of dietary interference within this timeframe.

3.2 MEDICATION INTERFERENCE

Pharmaceutical interference analysis identified multiple drug classes affecting test results (Table 4). False-positive results were associated with hormonal drugs, amino acid supplements and protein drugs, corticosteroids and glucocorticoids, certain traditional medicines, and central nervous system medications.

False-negative results were linked to tyrosine inhibitors, salicylic acid derivatives, vitamin C supplementation, sedatives and analgesics, and antihypertensive medications.

3.3 PHYSIOLOGICAL AND PATHOLOGICAL INTERFERENCE

Certain physiological states and pathological conditions affected test accuracy. False-positive results were observed in individuals experiencing intense physical exercise, trauma, hypoxia, bleeding, or extreme fatigue. False-negative results were more common in patients with diabetes, gastritis or gastric ulcers (particularly with *Helicobacter pylori* infection), excessive hydration, or advanced-stage cancer. Any condition causing abnormal urine coloration invalidated test results.

4. DISCUSSION

This comprehensive evaluation of a colorimetric urinary tyrosine detection method demonstrates sensitivity of 96.69% and specificity of 99.40% for malignant tumor detection in a large patient population. These findings warrant examination in the context of existing literature and established diagnostic approaches.

The observed sensitivity of 96.69% for malignant tumor detection in this study population exceeds that reported for several established tumor markers. Carcinoembryonic antigen (CEA) for colorectal cancer demonstrates sensitivity of 30-70%

(Duffy et al., 2007; Locker et al., 2006), cancer antigen 125 (CA-125) for ovarian cancer shows sensitivity of 50-80% (Bast et al., 2009; Menon et al., 2009), and prostate-specific antigen (PSA) for prostate cancer exhibits sensitivity of 70-90% with noted specificity limitations (Catalona et al., 1991; Thompson et al., 2004). However, direct comparison is complicated by differences in study populations, cancer stages, and methodological approaches.

The method's detection of diverse cancer types suggests identification of a metabolic alteration common to malignancy rather than cancer-specific markers. This broad detection capability presents both potential advantages for comprehensive screening and limitations regarding tumor localization, necessitating additional diagnostic procedures for positive results.

The elevation of urinary tyrosine in cancer patients aligns with documented alterations in cancer metabolism. Malignant cells exhibit altered amino acid metabolism, characterized by increased protein turnover, dysregulated enzyme activity, and metabolic reprogramming (Lieu et al., 2020; Phang et al., 2015). Tyrosine serves as precursor for catecholamines and melanin, both potentially altered in malignancy (Eisenhofer et al., 2004; Slominski et al., 2004).

Several mechanisms may contribute to elevated urinary tyrosine: increased protein catabolism in tumor tissue, altered tyrosine aminotransferase activity, tumor-induced systemic stress response elevating catecholamine production, and impaired hepatic metabolism (Holecek, 2010; Mayers et al., 2014). The consistent elevation across diverse cancer types suggests these mechanisms represent common features of malignant disease.

The correlation with HPLC ($r=0.94$), particularly in high-concentration ranges (0% deviation for >500 mg/L), supports the analytical validity of the colorimetric method. HPLC remains the reference standard for amino acid quantification (Kaspar et al., 2009; Armenta et al., 2010). However, HPLC requires specialized equipment, trained personnel, sample preprocessing, and extended analysis time (Shimbo et al., 2009).

The 11.4% maximum deviation in low-concentration ranges has limited clinical impact as these concentrations fall within or near the negative range. The concordance in high-concentration ranges where clinical decision-making is most critical supports reliability for identifying high-risk patients.

4.1 INTERFERENCE FACTORS AND LIMITATIONS

The characterization of interference factors provides important information for test implementation. The finding that dietary interference resolves within 48 hours enables evidence-based patient preparation protocols. The 23.3% false-positive rate from seafood consumption is preventable through appropriate patient instruction.

Medication interference presents challenges, as many interfering drugs cannot be safely discontinued. For patients on these medications, alternative screening approaches or careful clinical correlation becomes necessary. The test's unsuitability for patients with diabetes, *H. pylori*-associated gastritis, or conditions causing abnormal urine coloration limits applicability.

4.2 COMPARISON WITH OTHER URINARY BIOMARKERS

Several urinary biomarkers have been developed for specific cancers.

Nuclear matrix protein 22 (NMP22) and bladder tumor antigen (BTA) for bladder cancer show sensitivities of 40-70% with specificities of 60-90% (Lotan and Roehrborn, 2003; Chou et al., 2015). Urinary prostate cancer antigen 3 (PCA3) for prostate cancer demonstrates sensitivity of 60-70% and specificity of 70-80% (Haese et al., 2008; Roobol et al., 2010).

The evaluated method shows higher sensitivity (96.69%) in this study population compared to these cancer-specific urinary biomarkers, though direct comparison is limited by differences in study design and populations. The method's lack of cancer-type specificity distinguishes it from these targeted biomarkers.

Implementation of this test requires consideration of several factors:

1. **Target Population:** The method may be most appropriate for asymptomatic individuals at moderate cancer risk in settings where the observed performance characteristics are applicable.
2. **Clinical Workflow:** Positive results should trigger structured diagnostic pathways including detailed history, physical examination, and appropriate imaging or tissue sampling. The test should not replace established cancer screening protocols.
3. **Patient Education:** Clear communication regarding test limitations, interference factors, and the need for confirmatory testing is essential.
4. **Quality Control:** Standardization of reagent preparation, color scale interpretation, and result reporting is crucial for maintaining diagnostic accuracy across settings.
5. **Cost-effectiveness:** Comprehensive cost-effectiveness analysis must consider costs of follow-up procedures for positive results and comparison with alternative screening strategies.

4.3 STUDY STRENGTHS AND LIMITATIONS

Study strengths include large sample size (n=8,078), diverse disease representation, multiple validation methods (HPLC, spectrophotometry), and systematic interference factor assessment.

Several limitations warrant consideration: (1) the study population was limited to individuals aged 18-60 years in China, performance in other populations requires validation; (2) cancer stage information was not consistently reported, precluding analysis across disease stages a critical consideration for screening applications; (3) the study design was diagnostic accuracy assessment rather than prospective screening evaluation, performance as a screening tool in asymptomatic populations requires dedicated prospective studies; (4) the lack of cancer-type specificity necessitates additional diagnostic procedures for all positive results; (5) long-term follow-up data on false-negative cases are unavailable, leaving uncertainty about whether negative results in cancer patients reflected early disease or test limitations.

4.4 RESEARCH NEEDS

Several research priorities emerge from this evaluation:

- Prospective screening studies in asymptomatic populations to assess performance as a screening tool;
- Analysis of test sensitivity across cancer stages;

- Evaluation of combination biomarker approaches;
- Validation in diverse populations (age, ethnicity, geography);
    - Investigation of mechanisms underlying elevated urinary tyrosine;
    - Development of approaches to reduce interference;
    - Comprehensive cost-effectiveness analysis.

5. CONCLUSION

The evaluated colorimetric urinary tyrosine detection method demonstrates sensitivity of 96.69% and specificity of 99.40% for malignant tumor detection in this study population. The method shows strong correlation with HPLC, particularly in high-concentration ranges.

Key findings include significantly higher positive rates in malignant tumors (96.69%) compared to benign conditions (3.35%) and healthy individuals (0.60%), resolution of dietary interference within 48 hours, and broad detection across multiple cancer types.

The method's limitations include lack of cancer-type specificity, medication interference, unsuitability for certain patient populations, and need for confirmatory diagnostic procedures for positive results. The test should be positioned as a potential screening tool requiring further validation rather than a definitive diagnostic test.

The semi-quantitative colorimetric approach presents characteristics that may be suitable for certain clinical applications, though implementation requires careful consideration of the documented limitations and interference factors. Future research should focus on prospective screening trials, cancer stage-specific analysis, and comprehensive evaluation in diverse populations and clinical settings.

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